Mental Health Co-morbidity in Children and Adolescents with Fetal Alcohol Spectrum Disorder

By

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Abstract

Children and adolescents with Fetal Alcohol Spectrum Disorder (FASD) present with a range of physical, mental, behavioral, and cognitive challenges which can result in poor long-term outcomes. Mental health issues affect over 90% of individuals with FASD and is the most common and pressing secondary problem affecting children and adolescents with FASD or prenatal alcohol exposure (PAE). I examined the pattern and rates of mental health disorders diagnosed, the role of risk and protective factors on these outcomes, and the impact of having a mental health co-morbidity upon neurobehavioral functioning in children and adolescents with FASD/PAE.

In Study 1, I retrospectively examined the prenatal and postnatal risk factors associated with internalizing and externalizing mental health disorders diagnosed in a large sample of children and adolescents (n = 209) aged 3 to 17 years assessed for an FASD. Findings revealed that 54.8% of our sample were diagnosed with a mental health disorder, and up to 33.3% were at-risk for a mental health diagnosis. The most common co-morbidities reported in our sample included ADHD (46.9%, n = 98), Anxiety (10.5%, n = 22), Attachment Disorder (9.6%, n = 20), ODD or Conduct Disorder (7.7%, n = 16), PTSD (7.7%, n = 16), and Depression (6.2%, n = 13). Children with a history of 4 or more Adverse Childhood Experiences (ACEs) were at 4 times increased risk for having an internalizing mental health diagnosis. Age at assessment and exposure to abuse or neglect emerged as significant risk factors for an internalizing disorder, while sleep issues, gestational weight, drug use during pregnancy, and number of pregnancies emerged as significant risk factors for an externalizing disorder. Living in a two-parent home emerged as a protective factor associated with an externalizing disorder, whereas living in a non-fostercare placement at the time of FASD assessment, biological parent history of behavioral

issues or legal issues, and lower intellectual ability, were identified as protective factors associated with an internalizing disorder. Protective factors identified in this study as being associated with positive mental health outcomes are most likely due to receiving increased supports and services.

In Study 2, I compared the neurobehavioral profile of 24 children and adolescents with FASD/PAE, aged 9 to 19 years, with and without a mental health co-morbidity. Children and adolescents with a mental health co-morbidity showed trends towards greater difficulty on measures of executive function, memory and learning, attention, and behavior. Parent reported executive behavior difficulties correlated with increased behavioral problems measured on two mental health rating-scales.

Results from this research have important implications for improving mental health screening and care among children and adolescents with FASD. Future directions and implications regarding mental health outcomes among children and adolescents with FASD are discussed.

Keywords: FASD, prenatal alcohol exposure, childhood, mental health issues, co-morbidity, risk factors, neurobehaviour, executive functions

PREFACE

This dissertation is original, unpublished, independent work conducted by the author, Sukhpreet Tamana. The research projects of which this is part of received ethical approval from the University of Alberta Research Ethics Board. 'Risk and Protective Factors for Secondary Diagnoses in Fetal Alcohol Spectrum Disorders,' Pro00043905, March 3rd/2014 and renewed February 10th/2015, and 'Neurobehavioral Functioning in Children with FASD or PAE and Mental Health Co-morbidity,' Pro00042537, Pail 14th/2014 and renewed March 17th/2015. Both projects received operations approvals from the Glenrose Rehabilitation Hospital.

DEDICATION

In loving memory of my grandmother

Dadi Gurbachan Kaur Shoker

Dedicated to all those families who are raising a child with unique talents and needs

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When one door closes, another opportunity opens.

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GLOSSARY OF TERMS

FASD: Fetal Alcohol Spectrum Disorder.

PAE: Prenatal Alcohol Exposure.

PAE Group: Individuals with confirmed prenatal alcohol exposure but did not meet criteria to receive a full FASD diagnosis.

Co-morbidity: Diagnosed with one or more disorders in addition to having FASD/PAE.

MH: Mental Health.

EXT: Externalizing mental health disorder.

INT: Internalizing mental health disorder.

EF: Executive functions.

CHAPTER I

Introduction

Prenatal alcohol exposure (PAE) is a leading preventable cause of birth defects, developmental disorders, and mental retardation (American Academy for Pediatrics of Substance Abuse and Committee on Children's Disabilities, 2000), and is recognized as a teratogen affecting physical dysmorphology, growth, and neurobehavioral outcome (Jacobson, Jacobson, Sokol, Martier, & Ager, 1993). The incidence of Fetal Alcohol Spectrum Disorder (FASD) occurs at an alarming rate of 2 to 5 per 100 children in the United States and some Western European Countries (May et al., 2009). Although there are no statistics on the prevalence of FASD in Canada or Alberta, researchers estimate that FASD occurs in 1 in 100 live births (Alberta Alcohol & Drug Abuse Commission, 2004; Health Canada, 2007; Stade, Ungar, Stevens, Beyene, & Koren, 2006) making this a public epidemic of great concern (Chudley et al., 2005). FASD is a significant health concern that requires extensive support and services and poses challenges for the Canadian health care system (Popova, Lange, Burd, & Rehm, 2012). Individuals with FASD require supports and services encompassing healthcare, social services, education and training, justice system, addictions, and family support services (Alberta Children Services, 2006). The economic and quality of life costs of FASD in Canada are estimated to range from 1-2 million per child for lifelong care and support (Stade, Ungar, Stevens, Beyen, & Koren, 2007). FASD has implications for the affected person, the biological mother, family, and community (Chudley et al., 2005).

FASD is an umbrella term used to describe a range of physical, behavioral, emotional, social functioning deficits, and neurobehavioral impairments including cognitive, neuropsychological, behavioral, and adaptive impairments that result from PAE (Chudley et al.,

2005). Many children with FASD have been identified as being at significant risk for a co-morbid mental health disorder. Mental health is an especially pressing health concern for children with FASD and their families and poor outcomes in terms of mental health have been documented in many of these children (Pei, Denys, Hughes, & Rasmussen, 2011). Mental health disorders are reportedly found in 90% of individuals with FASD (Pei et al., 2011), and affecting 94.2% of children and adolescents with FASD involved with the child welfare system (Chasnoff, Wells, & King, 2015), and between 88% to 67% and 77% to 67% Canadian children diagnosed with FASD or prenatal alcohol exposure but no FASD diagnosis (McLaughlin et al., 2015; Rasmussen et al. 2013; Tamana et al. 2015). In particular, externalizing mental health disorders such as Attention Deficit and Hyperactivity Disorder (ADHD) and conduct disorder (CD), as well as internalizing mental health disorders such as anxiety, depression, and mood co-morbidities are overrepresented in this population (Pei et al., 2011). Many of these co-morbidities increase risk for suicide and involvement in youth justice services and if misunderstood can lead to inappropriate remediation and intervention strategies (Pei et al., 2011; Rasmussen, Andrew, Zwaigenbaum, & Tough, 2008). Therefore, it is imperative to understand whether these diagnoses are an appropriate representation or reflects a more complex relationship between brain-based and environmental factors (Pei, et al., 2011).

Prior research has focused on identifying the prevalence of mental health issues in children with FASD or PAE or establishing a dose-response relationship between PAE and mental health behaviors in childhood. In an attempt to gain a more comprehensive understanding of the impact of mental health co-morbidity in children with FASD researchers have begun to study the neurobehavioral profile in children with FASD in comparison to other clinical groups. More specifically, research has compared the neurobehavioral profile in children with FASD

and/or FASD/ADHD to children with only ADHD (Mattson, Crocker, & Nguyen, 2011). However, this same in depth understanding of how other common mental health co-morbidities present in FASD such as Oppositional Defiant Disorder (ODD), CD, depression, and anxiety has not been examined. Presently, there is a little information that addresses whether the neurobehavioral functioning of children with FASD differ in the presence of other co-morbid mental health issues. This information is essential to informing the relationship between FASD and co-morbidity with other disorders.

Moreover, the high prevalence of mental health co-morbidities among children with FASD likely reflects an interaction effect between PAE and multiple environmental and biological risk factors that are known to impede typical development in non-exposed children. In particular, multiple adverse prenatal (Flynn, Berman, & Marcus, 2009; Coyne, de Costa, Heazlewood, & Newman, 2008) and postnatal (Streissguth et al., 2004) risk factors have been noted in this population and are likely critical to the observed prevalence of mental health issues in these children. Relatively few studies have explored the influence of risk and protective factors and particularly prenatal or biological factors on mental health co-morbidity in FASD. Research using large datasets, examining both prenatal and postnatal factors together, comparing children with FASD to children with PAE that are imperative for identifying critical risk and protective factors for persistent or severe mental health co-morbidities are lacking but could be helpful for developing unique and novel intervention strategies.

Researchers have stressed the need for follow-up studies of poor mental health outcomes and the need to understand factors that could help build resiliency against mental health co-morbidities in this population (Pei et al., 2011; Paintner, Andrew, & Burd, 2012). The paucity of research in this area is disconcerting and there exists a gap in provision of evidence-based mental

health care services for this population. Research in this area is urgently required to provide knowledge that could support evidence-based practices for recognizing and addressing mental health issues in children with FASD. Although there has been some research completed in this area, very little research has examined factors mediating mental health issues or the relation between neurobehavioral function and co-morbidity with other disorders. This information would be particularly helpful for early and effective diagnosis that would enable early and accurate identification of mental health co-morbidities and would help direct interventions appropriately. Therefore, the goals of this thesis were to first review relevant literature about typical neurodevelopment and atypical neurodevelopment in FASD (chapter 2), second, explore prenatal and postnatal risk factors associated with mental health co-morbidity in children and adolescents with FASD (chapter 3), and third, examine the neurobehavioral profile among children and adolescents with FASD with and without mental health co-morbidity (chapter 4).

CHAPTER II

Background and Literature Review

Overview

In developmental psychology, it is now widely viewed that children thrive in a supportive and optimal environment and those children who grow under adverse circumstances can fail to thrive. There is however one exception, in that children are differentially susceptible to their environment. One theory posits that the *dandelion* may be a resilient child that responds well even in the face of stress or adversity or the *orchid* child may initially suffer severely but flourish spectacularly when receiving care (Belsky & Pluess, 2009; Belsky, Bakermans-Kranenburg, & Uzendoom, 2007; Ellis & Boyce, 2005). In this regard, both genetic and environmental influences are likely important to supporting neurodevelopment. Therefore, a biopsychosocial perspective (Bronfenbrenner & Ceci, 1994) can provide an important context for the course of neurodevelopment in FASD. This section will present two main themes: typical neurodevelopment and atypical neurodevelopment in FASD. This first section begins with a basic review of background information on typical neurodevelopment highlighting the role of the frontal lobe and higher order cognitive abilities (known as executive functioning; EF). This is followed by information about the prevalence of childhood mental health issues in general populations and the importance of risk and protective factors in mental health outcomes. The final section will discuss atypical neurodevelopment in FASD focusing on the neurobehavioral consequences with particular emphasis on deficits in EF and vulnerability for mental health co-morbidity in this population. Finally, existing literature comparing children with FASD with and without mental health co-morbidity on EF and other neurobehavioral measures will be critically reviewed in order to identify appropriate research questions. The section will end with an

introduction to the current study that involved a retrospective and a prospective examination of mental health co-morbidity in children and adolescents with FASD or PAE.

Typical Neurodevelopment

Brain and function. ***Developing brain***. In the prenatal months, a significant period of brain development takes place that begins in approximately the third week of gestation and continues into early adulthood (Kolb & Whishaw, 2010). Several key events in brain development exist that occur in a predetermined sequence between weeks 4-20, when neurulation (formulation of the neural tube) occurs, from which eventually evolves the Central Nervous System (CNS) (forebrain and facial structures, the brain and ventricles, and the spinal cord), followed by generation, proliferation, and migration of cell neurons. Migration of cells contributes to cortical thickness through movement within the cortex via glia cells (Rakic, 1990) and neural pathways develop via axonal growth development enabling connections between neurons to promote neuron function and survival. In the last trimester of gestation, synaptogenesis (establishment and pruning of the neurocircuitry), myelination (insulation of neurons to form white matter tracts) and begin and continue to late adolescence.

During the postnatal period (birth-adulthood), rapid changes in myelination (white matter axon tracts), gyrification (increase in surface area and grey matter), and neurochemical structures take place and are essential to the brains functional capabilities (Kolb & Whishaw, 2010). Cross-sectional and longitudinal magnetic resonance imaging (MRI) studies confirm peaks in grey matter within subcortical regions for the basal ganglia by early childhood (7-9 years) and cortical regions for the temporal, parietal, and frontal lobes by middle childhood (10-12 years) (Lenroot & Giedd, 2006). Cortical development within the temporal, parietal, and frontal regions follow a pattern of development that emerge in the primary areas first followed by secondary areas

involved in more complex processing (Lenroot & Giedd, 2006). However, the frontal lobes continue to develop throughout childhood and adolescence and into early adulthood with the most noticeable changes occurring within the dorsal-lateral regions that subserve higher cognitive abilities involved in decision-making (Lenroot & Giedd, 2006); consistent with developmental patterns of higher cognitive abilities (i.e. EFs) emerging in later development (Casey, Tottenham, Liston, & Durston, 2005). Distinct neurobehavioral differences between children, adolescents, and adults are in part attributed to changes in neural circuitry involving the frontal lobe (Zelazo, Carlson, & Kesek, 2008).

Frontal lobe and executive functions. The frontal lobe is a brain region most relevant to higher-order cognitive functions following a maturational course extending into adolescence and comprises a number of sub-regions including the orbitalfrontal, ventrolateral, dorsolateral, and rostrolateral prefrontal cortices. The frontal lobe plays a crucial role in the neural systems that support EFs (Zelazo, Carlson, & Kesek, 2008; Stuss & Knight, 2012; Welsh & Pennington, 1988). EF is referred to as higher order cognitive abilities composed of multiple, related cognitive skills (Miyake et al., 2000) that lead to achievement of goal directed behavior under conscious control (Zelazo & Muller, 2002). EF involves multiple cognitive processes including planning, organized search, inhibition, working memory, set shifting, flexible thinking, strategy employment, and fluency (Welsh & Pennington, 1988; Welsh et al., 1991). Growth in EF is supported by frontal cortex maturation evidenced by changes in neural circuitry involving the prefrontal cortex (PFC; Zelazo & Muller, 2002), and in particular myelination of white matter tracts between prefrontal and posterior frontal regions (Nagy, Westerberg, & Klingberg, 2004). Developments in the PFC follow a prolonged developmental course in critical periods of PFC maturation throughout the course of child development (Stuss & Knight, 2012). Consequently,

common regions that subserve EF in childhood, adolescence, and adulthood show age-related changes in patterns of activation (Casey et al., 2005).

Case studies of brain patients with damage to specific neuroanatomical pathways mediated by the frontal cortex show impaired abilities on tasks assessing EF (Damasio, 1994). Different neuroanatomical substrates mediate two types of EF that involve cognition-based EF (Cold EF) and emotion-based EF (Hot EF) (Zelazo & Muller, 2002; Kodituwakku, Kalberg, & May, 2001). Cognition-based EF is involved in problem solving, planning, set-shift, fluency, and working memory mediated by the dorsolateral prefrontal cortex; and emotion-based EF is mediated by the orbitalfrontal cortex and involved in decision-making, processing affective/non-affective stimuli, and responses to reward and punishment stimuli (Zelazo & Muller, 2002; Kodituwakku, et, al., 2001). However, most developmental research has been conducted on cognition-based EF therefore cognition-based EF will be the focus of discussion in the following section.

Executive function and development. The timeline of EF development is in accordance with Piaget's theory of cognitive development (1964). Piaget's theory characterized that children acquire knowledge through sequential stages by adapting mentally to their environment through accommodation and assimilation processes (Piaget, 1964). A child would follow four sequential stages of cognitive development from birth to adolescence: sensorimotor (birth to 2 years), preoperational (2 to 7 years), concrete operational (7 to 9 years), and formal operational (early adolescence) (Piaget, 1964). The development of EF seems to be consistent with Piaget's theorized age of transitions particularly developmental changes in maturation in the frontal lobes (Stuss & Knight, 2012). Empirical research supports a hierarchical view of EF development (Zelazo, et al., 2008) that is likely governed by a child's ability to formulate rules with increased

complexity, to hold information in WM, and to problem-solve using these rules (Zelazo et al., 2002).

EF emerges early on during the first years of life (e.g. Diamond, 1990a, 1990b; Welsh & Pennington, 1988). In a series of studies conducted by Diamond and Goldman-Rakic, (1989) they demonstrated that infants show successful performance on the Piagetarian A-not-B task by one years of age, a task analogous to the object-delayed task associated with prefrontal region in non-human primates. In both tasks, the object is hidden in the same location over a number of repeated trials, and for the critical trial, the object is hidden in a new location in front of the participant. A successful trial is evident when the infant/non-human primate no longer perseverates, which is thought to indicate maturation in the PFC region (see Welsh & Pennington, 1988, for a review). Many studies have reported rapid changes that emerge in EF early on and several EF tasks have been noted for detecting developmental spurts in EF functions between age two and five years (see Garon, Bryson, & Smith, 2008). For example, the Dimensional Change Card Sort (DCCS) task measures switching in young children and the child is asked to sort cards according to shape and then after a number of consecutive trials the child is asked to sort cards according to color (or vice-versa). Children younger than 3 years of age fail the DCCS Task but children age 4 and over are able to switch from the first rule to the second rule suggesting an early milestone in EF development (see Zelazo et al., 2006 for a review) that appears to align with early frontal cortex maturation (Moriguchi & Hiraki, 2009; 2011; Nagy, et al., 2004). Furthermore, some adult EF abilities begin to emerge between six and twelve years of age, including visual search, impulse control, inhibition, and set shifting (Zelazo & Muller, 2002). EF abilities involving verbal fluency and planning continue to develop into adulthood (Zelazo & Muller, 2002).

As mentioned earlier, theoretical accounts of the development of EF abilities confer a hierarchical approach to EF development (Zelazo, Carlson, & Kesek, 2008). Since multiple related cognitive abilities are involved in EF, researchers have employed confirmatory factor analysis (CFA) in an attempt to examine the underlying latent variable or construct that represents a 'purified' EF measure. In early childhood it would appear that a unitary model best accounts for correlations between working memory, shifting (cognitive flexibility), and inhibition (Wiebe et al., 2011; Wiebe, Espy, & Charak, 2008; Willoughby, Blair, Wirth, & Greenberg, 2010; Willoughby, Wirth, & Blair, 2011), whereas, the EF structure in later childhood (Alloway, Gathercole, Wills, & Adams, 2004; Lehto. Juujaervi, Kooistra, & Pulkkinen, 2003; Gathercole, Pickering, Ambridge, & Wearing, 2004) and adulthood (Miyake et al., 2000) has consistently been found to involve three distinct but correlated factors that include working memory, inhibition, and shifting (cognitive flexibility) (Miyake & Friedman, 2012). This suggests the unity and independence of the three EF factors may change developmentally in a way that is likely fundamental to transition toward separable adult like EF abilities (Garon et al., 2008), guiding higher order EF abilities such as problem solving, reasoning, and planning (Diamond, 2006).

In short, neurodevelopment continues throughout childhood and adolescence with the most critical changes occurring in the brain regions most relevant to EFs. EF has an important role in child development because these higher cognitive abilities involve reasoning, problem solving, planning, self-regulation, behavior, emotion, and personality, each fundamental to daily living. Developmental changes in EF abilities align with how children develop in their thinking, adaptive and life skills, social functioning, emotion, and behavior, as they grow older. Specifically researchers have found that children with good EF abilities have better school

success (e.g. Morrison, Ponitz, & McClelland, 2010), better quality of life (e.g. Davis, Marra, Najafzadeh, & Lui-Ambrose, 2010), less social problems (e.g. trouble with the law, recklessness, emotional outbursts) (Denson, Pederson, Friese, Hahm, & Roberts, 2011), and are at less risk for mental health issues such as Attention Deficit Hyperactivity Disorder (ADHD) (e.g. Diamond, 2005), conduct disorder (CD) (e.g. Fairchild et al., 2009) depression (e.g. Taylor-Tavares et al., 2007), and schizophrenia (e.g. Barch, 2005) (see Diamond, 2012 for a review). Furthermore, the environment in which typical neurodevelopment occurs can profoundly influence capacity for EF and hence functioning in many areas of daily life especially mental health issues.

Child Development and Mental Health

Mental Health in Childhood. A mental health issue can be best described as a psychiatric condition (behavioral or psychological) marked by significant distress or impairment in daily functioning (American Psychological Association (APA), 2000). Furthermore, mental health issues have recently been re-conceptualized to include a clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects dysfunction in psychological, biological, or developmental processes underlying mental functioning (APA, 2013). In the general population, mental health disorders are common with the prevalence varying between 2% and 6% (APA, 2013), with first onset usually occurring in childhood or adolescence (Kessler et al., 2005). Between 12% and 22% of children and adolescents are reported to exhibit a significant mental health issue and these rates appear to increase with developmental age (Kessler, et al., 2005). In Canada, an estimated incidence of 13% to 18% of Canadian children and adolescents (greater than 1 million Canadian youth) suffer from a mental health disorder (Costello, Mustillo, & Erkanli, 2003; Waddell, Offord, Shepherd, Hua, & McEwan, 2002). Approximately one-half of all lifetime cases of mental health disorders begin

by age 14 and three-fourths by age 24 (Kessler, et al., 2005). Untreated mental health issues tend to persist leading to substantial functional impairment throughout life (Kessler et al., 2005). The range of mental health disorders experienced by children and youth include depression, anxiety, ADHD, CD, Oppositional Defiant Disorder (ODD), and even more severe psychopathology such as mood disorder, psychosis, and substance use disorder.

Childhood mental health issues are typically classified into two groups: *externalizing* and *internalizing* psychopathology (Achenbach, 1981). Achenbach and Edelbrock, (1978) define internalizing behaviors (i.e. anxious, withdrawn, depressed behavior) as a way of adapting to an environment that causes internal stress, whereas externalizing behaviors (i.e. aggressive and rule-breaking behavior) are best defined as acting outwardly in a manner that causes conflict with others (Achenbach & Edelbrock, 1978). Internalizing psychopathology refers to depression, anxiety, and mood disorders whereas externalizing psychopathology refers to behavioral or emotional dysregulation disorders such as CD, ODD, and ADHD. Several studies have reported gender differences in rates of internalizing and externalizing disorders in childhood and adolescence (Kessler et al., 2005). In particular researchers note that males display greater externalizing issues such as ADHD, CD, and ODD than females in childhood and these lessen in adolescence, whereas internalizing issues are similar for boys and girls in childhood but are higher for girls than boys in adolescence particularly anxiety and depressive disorders (Kessler et al., 2005; Merikangas et al., 2009).

Children diagnosed with one mental health disorder are often found to have a number of other disorders in addition to this diagnosis, formally referred to as ***co-morbidity*** (Feinstein, 1970). The term ‘co-morbidity’ asserts clinical significance by specifying that not all symptoms can be accounted for by one diagnostic category (Feinstein, 1970). Pennington et al. (2005)

noted that co-morbidity potentially has implications for theoretical and clinical insight. First, their presence may influence the course and treatment of another disorder (Caron & Rutter, 1991). Second, exploring co-morbidity can determine whether presence of a specific cluster of symptoms is associated with a given disorder or a co-morbid condition, and can lead to improved validity of a diagnostic criterion (Caron & Rutter, 1991). Finally, where two disorders commonly co-occur this implies to some extent there may be a degree of overlap between them (Caron & Rutter, 1991; Pennington, Willcutt, & Rhee, 2005). Thus, investigating the relationship between two co-morbid disorders may assist in identifying underlying mechanisms that can offer a theoretical explanation of a co-morbid disorder (Pennington, et al., 2005), but also inform appropriate treatment for alleviating co-occurring symptoms.

Diathesis-stress model. The Diathesis-Stress model proposes that exposure to multiple stresses over the lifetime increases susceptibility for developing a psychological condition that interferes with daily living (Ingram & Luxton, 2005; Zuckerman, 1999). Similar to a biopsychosocial perspective, the model considers predisposing, precipitating, and perpetuating factors and their interaction with onset of psychopathology (Ingram & Luxton, 2005; Zuckerman, 1999). In this regard, diathesis-stress infers that some individuals have a predisposition or vulnerability to developing a psychopathological disorder due to interactions between biological-genetic vulnerability and environmental stressors (Zuckerman, 1999). Therefore, mental health disorders manifest in individuals predisposed to family history or genetic origin (i.e. specific gene), behavioral or temperamental characteristic, or physiological or endophenotypic nature (heritable trait associated with an increased risk for a disorder), combined with a *heightened sensitivity* to environmental stressors (Belsky & Pluess, 2009; Zuckerman, 1999). In other words, the onset of mental health psychopathology is not a simple gene and

environment interaction (GXE; Gottesman & Handson, 2005) rather other complex mechanisms are also involved in the onset of a mental health disorder. Henceforth, researchers have documented poor mental health outcomes in children exposed to familial risk, and/or adverse stressors during pregnancy, at birth, and in postnatal life.

Extensive research has shown that familial genetic factors increase risk for developing a mental health disorder in later life. Most of the evidence originates from genetic studies of children with and without the phenotype (expression of a condition). There is considerable evidence that certain childhood disorders such as autism, downs syndrome, cerebral palsy, or dyslexia are associated with hereditary factors. For example, twin studies of children with autism and their siblings have found high concordance rates of 60-90% in identical twins (Gottesman & Hanson, 2005). Furthermore, genetic studies of mental health disorders indicate that having a first-degree relative diagnosed with a mental health disorder increases the chance of developing a mental health condition such as schizophrenia (Gottesman & Gould, 2003). Similarly, maternal history of depression increases risk of developing depression in childhood, later adult life (Birmaher et al., 1996), or during the postpartum period (Viguera et al., 2011). There is also significant overlap between numerous childhood disorders. For example, follow-up studies of children with ADHD indicate that these children are frequently diagnosed with CD, ODD, anxiety, major depressive disorder (MDD), or bipolar disorder and that 20-25% of these children have a diagnosis for a learning disorder (Pliszka, 2000). However, the development of a mental health issue is often preceded by other risk factors such as a stressful or significant life event (Ingram & Luxton, 2005; Zuckerman, 1999).

Prenatal experiences may influence later psychological outcomes (Welberg & Seckl, 2001). There is growing evidence in support of the concept of fetal programming whereby fetal

or early life experiences (i.e. environmental or non-genetic) can permanently alter physiological and behavioral systems (Welberg, Seckl, & Holmes, 2001). Thus, the interplay between environment and biology during early life environmental changes likely alter genetic expression (via epigenetic processes) therefore increasing susceptibility to disease or disorder in later life (Archer, Berninger, Palomo, & Kostrzewa, 2010; Champagne & Curley, 2009; Szyf, 2009). As a result, prenatal or early postnatal risk factors may be early markers of poor fetal growth effects and later poor outcomes (Welberg & Seckl, 2001). For example, studies have shown that low birth weight is related to hypertension or type-II diabetes in later adult life (Barker, 1992; Barker, 1999) and prenatal stress may alter the HPA system important to depression and anxiety (Welberg & Seckl, 1998; Zhang, Sliwowska, & Weinberg, 2005).

Studies of mental health stressors have identified a number of early risk and protective factors. In particular, specific pre- and perinatal (at-birth) risk factors have been associated with mental health issues such as lower socio-economic status (SES), birth complications, prenatal stress experience, and maternal mental health (see Hackman et al., 2010 for a review). It is also clear that some of these risk factors have been implicated in later childhood mental health diagnoses and some of the most common findings include 2-fold increased risk for schizophrenia following birth complications (Gottesman & Gould, 2003), and ADHD following pre- and perinatal complications (Galera et al., 2011; Pineda et al., 2007; Linnet et al., 2003). Allen, Lewinsohn, and Seeley (1998) using retrospective data explored the relationship between pre- and perinatal histories and later risk for psychopathology in 579 adolescents (aged 4-18 years). Their findings revealed that major depression was associated with maternal emotional problems during pregnancy; anxiety related to fever and illness during the first year of life and maternal history of miscarriage and still-birth; disruptive disorders (i.e. ODD) related to poor emotional

health during pregnancy and birth complications; and substance-use disorder related to maternal use of substances during pregnancy (Allen et al., 1998). Although these results were based on maternal recall when the child was between 14 to 18 years old, other studies based on prospective data have found similar results in relation to child behavioral and emotional issues (Robinson et al., 2008; Linnet et al., 2003).

Robinson et al. (2008) followed up on a large cohort of preschool children and parents completed a measure of behavioral and emotional mental health issues (i.e. Child Behaviour Checklist). Antenatal factors such as younger maternal age, SES, maternal exposure to multiple stress events, maternal smoking, and ethnicity were independently associated with later externalizing and/or internalizing problem behaviors. Interestingly, the authors proposed that prenatal exposure to stressful life events could lead to excessive exposure to cortisol during prenatal development hence inattentive and externalizing behaviors may represent a child's adaptation to a stressful environment (Robinson et al., 2008). Another plausible explanation could be in relation to maternal mental health also known to have implications for a child's later internalizing problem behaviors (O'Connor Heron, Golding, Beveridge, & Glover, 2002). Similarly, Ownes and Hinshaw (2013) found that perinatal problems such as breathing problems, early labor, and birth complications was associated with childhood co-morbid depression among children with ADHD, even after controlling for SES and maternal symptoms of ADHD and depression. However, their findings did not reveal an association between perinatal problems and other co-morbid childhood psychiatric problems such as anxiety or externalizing problems (Ownes & Hinshaw, 2013). Together these findings imply that prenatal events and early postnatal life significantly affect later childhood mental health outcomes.

Research in human and animal studies has in addition to prenatal factors implicated child-caregiver relationship, SES, cognitive stimulation, and home environment in positive and negative development in later mental health (Hackman et al., 2010). The postpartum period is important for infant attachment and two key protective factors related to this period: positive caregiver-child relationships and emotional regulation (self-regulation abilities) (Zeanah, 1996). Early positive attachment can be a protective factor against later adverse environmental experiences (Rutter, Kreppner, & Sonuga-Barke, 2009). Studies by Meaney and colleagues (e.g. Fish et al., 2006; Liu et al., 1997) have shown that positive and negative parental behavior in rats during postpartum period modifies stress response and emotional function in offspring (see Hackman et al., 2010 for a review).

There has been increasingly more recognition that childhood experiences have important implications for poor childhood mental health, hence a child's environment plays a role in risk or resiliency for mental health issues. Researchers have shown that environmental experiences have both positive and negative effects on child development. By and large, children living in foster or residential care are at greater risk for behavioral problems and psychiatric issues (Bos et al., 2011; Maclean, 2003), poor attachment (Rutter, Kreppner, & Sonuga-Barke, 2009), and other adverse experiences such as poor academic performance and trouble with the law (Vinnerljung & Sallnas, 2008). Early social deprivation has long-term effects on the developing brain and mental health outcomes. For example, in a randomized control design, Bos et al. (2009) found that children living in institutionalized care show significant impairments on CANTAB measures of EF and visual memory, as compared to SES-matched control children. They also found that assignment to foster-care placement in early childhood was a significant predictor of spatial working memory (Bos, Fox, Zeanah, & Nelson, 2009). Furthermore, these same researchers have

shown that early foster-care placement has a positive effect (relative to children in institutionalized care) on memory function, externalizing problem behaviors such as ADHD (Guler et al., 2012), and later internalizing and externalizing mental health diagnoses (Bos et al., 2011).

Similarly, exposure to adverse childhood experiences such as abuse and exposure to violence has long-term effects on individuals, increasing the likelihood they may experience mental health issues later in life (see Chapman, Dube, & Adna, 2007). Adverse Childhood Experiences (ACE) provides operationalized criteria for measuring the presence of abuse and the accumulative impact of multiple childhood stressors (Felliti & Anda, 2009). For example, using data from the ACE study, Anda et al. (2006) examined the impact of ACE upon functioning in later adulthood. Their findings revealed a strong relationship between early adverse experiences and negative outcomes involving mental health, substance use, risky sexual behavior and aggression, impaired memory for episodic events, obesity, sleep disturbances and somatic complaints. Greater risk for negative outcomes was associated with higher accumulative ACE scores (Anda et al., 2006). Several ACE studies have reported that individuals that have experienced four or more categories, compared to those who have experienced none, have a 12-fold increase risk for poor health outcomes including drug abuse, alcoholism, depression and suicide (Anda et al., 2006; Felliti et al., 1999). Thus, ACEs show a graded relationship with to the presence of adult health outcomes. The poor mental health and physical outcomes associated with ACE underlines the important trajectory between childhood adversity and mental health and well being in later life. However, most previous research has focused on examining ACE in relation to long-term outcomes during adulthood, with few studies have considered ACE in relation to mental health issues and physical problems during childhood. Some recent work has

examined ACEs in relation to behavior (Burke et al., 2011) and physical health problems such as having poor health, somatic concerns, illness (Flaherty et al., 2013; Burke et al., 2011), and sleep problems (Chapman et al., 2009; 2011). One study examined ACE in an urban pediatric sample and found that those children with higher ACE scores, hence experienced more adversity, were more likely to have behavioral, learning, and physical health problems (Burke et al., 2011). However, the outcomes examined in the study were based on pediatrician reported measure of behavioral, learning, and physical health outcomes and not objective measures or confirmed diagnoses and therefore may not truly reflect the child's actual difficulties. More recently, in an attempt to determine whether some ACE co-occur more often than others during childhood and adolescence, Burke et al. (2013) examined the interrelation of ACEs in a large pediatric population. Their findings revealed that some ACEs co-occur increasing risk for exposure to another type of ACE. For example, both emotional and sexual abuse and living with one or no biological parents increases risk for exposure to physical abuse, even when controlling for other types of ACE (Burke et al., 2013). Similarly, recent work has reported on increased risk for ACEs among children diagnosed with ADHD, suggesting that exposure to trauma may influence ADHD diagnosis and management, which may have important implications for other pediatric mental health disorders (Brown et al., 2014).

Furthermore, other psychosocial risk factors that may be associated with childhood mental health outcomes have also been explored. For example, Kroes et al. (2002) found that low-level parental occupation, single-parent family, and occurrence of life event were the most important risk factors in differentiating between children with and without a mental health diagnosis. Moreover, low-level parental occupation was associated with CD, whereas living with a single parent and experiencing a significant life event was associated with mood and anxiety

disorders (Kroes et al., 2002).

Evidently, prenatal and postnatal risk factors have important implications for understanding risk for adverse outcomes such as childhood mental health disorders. It is important to note however that risk and protective factors rarely have a linear relationship with outcomes, rather cumulative effects of exposure to a combination of these factors can lead to poor mental health functioning (Zeanah, 1996). However, from late pregnancy throughout early years in life prenatal brain development is particularly vulnerable to biological and environmental influences. Owing to the fact that there exists critical periods in early brain development that can be influenced by environmental and biological factors and recent advances in research has revealed that environmental changes (both biochemical and social) can induce neurobehavioral alterations, as expressed in changes in intellect, cognition, behavior, adaptive abilities, social skills, and emotional regulation, and may produce long-term impairments in susceptible individuals. Hence, studying risk and protective factors have important implications for understanding mental health development in early childhood.

Brain and function in mental health. The brain's continuous development throughout childhood and adolescence makes it vulnerable to environmental stressors. Brain regions such as frontal lobe, hippocampus, and amygdala have been implicated in both internalizing and externalizing mental health disorders (see Mana, Paillere Martinot, & Martinot, 2010 for a review). In particular, the frontal lobe involved in EF is impacted by stress (Diamond, 2009) such that dopamine in the prefrontal cortex becomes elevated in response to mild stress (Roth et al., 1988). Thus, exposure to stress during neurodevelopment can result in aberrant brain changes that can lead to deficits in EF resulting in further functional impairments such as inattention,

slower processing, lower academic performance, poor social skills, and difficulties in adaptive and daily life abilities.

There is growing evidence that internalizing disorders may exacerbate neurobehavioral functioning. In particular, researchers have shown that children with internalizing mental health psychopathology display impairments on cognitive paradigms involving information processing. neurobehavioral impairments have also been documented on tasks involving perceptual processing, attention, and memory (see Semrud-Clikeman & Teeter-Ellison, 2009). Children with more severe mood disorders display impairments on EF tasks. For example, researchers have found that children with pediatric bipolar disorder display impairments on tasks involving working memory, attention, processing speed, and verbal memory and learning. However, some researchers have suggested that deficits in information processing appears to be more specific to bipolar disorder whereas other EF impairments may be attributed to the presence of co-morbidity with other childhood disorders (Mattis, Papolos, Luck, Cockerham, & Thode, 2011). Similarly, individuals with MDD show impairments on tasks of verbal learning and memory, focused attention, attention shifting, and error monitoring (Hasler, Drevets, Manji, & Charney, 2004). For example, Han et al. (2012) examined EFs in 31 adolescents with MDD (aged 14-19) as compared to 33 control children. They found that the MDD group showed impairments on tasks of sustained attention (i.e. CPT), decision-making (i.e. Iowa Gambling Task), and slower reaction times on an emotional go-no-go (Han et al., 2012). Although, some researchers have contended that neuropsychological impairments do not appear to be specific to childhood depression and may only reflect state dependent changes, other researchers have noted different neurobiological mechanism underlying some EFs such verbal working memory (Hasler et al., 2004).

Similarly, children with anxiety display deficits in attention processing of emotionally threatening word stimuli as demonstrated on adapted versions of the Stroop task and dot-probe task (see Ehrenreich & Gross, 2002 for a review). Furthermore, impaired cognitive abilities have also been noted on Wechsler Intellectual Scale for Children (WISC) subtests including digit span, arithmetic, and coding which suggests that anxiety disorders interfere with information processing, memory, and processing speed (Semrud-Clikeman & Teeter-Ellison, 2009). Researchers examining more severe anxiety disorders such as OCD have reported difficulties on tasks of EF involving response inhibition and decision-making (Olley, Malhim, Sachdev, 2007) and some of these impairments (e.g. cognitive flexibility and planning) appear to be independent of co-morbid depression and anxiety (Orstein, Arnold, Manassis, Mendiowitz, & Schachar, 2010). Evidently, it would appear that children with depression or anxiety show impairments on variety of information processing measures. Hence, the presence of internalizing disorders appears to exacerbate difficulties with neurobehavioral functioning in childhood and has implications for diagnosis and treatment.

EF deficits have been highly implicated in externalizing mental health disorders that include ADHD, CD, and ODD thus the presence of externalizing disorders likely has an impact upon functional outcomes. ADHD is a well-studied childhood disorder and there is substantial evidence to support EF deficits in attention, inhibition, set shifting, planning, and working memory (see Willicut et al., 2005 for a review). Although, there have been some discrepancies in these findings, some children with ADHD reportedly perform within the average range on neurobehavioral measures of inhibition and EF, perhaps because ADHD represents a heterogeneous group with multiple etiologies (Nigg et al., 2005). In addition, impairments on EF do not always correlate with behavioral measures of ADHD symptoms (e.g. Jonsdottir, Bouma,

Sergeant, & Scherder, 2006). Similarly, deficits in EF have also been associated with CD and ODD, particularly inhibition (Oosterlaan, Logan, & Sergeant, 1998). However, there have been some inconsistencies in the literature whereby some studies have only found EF deficits in children with ODD or CD that also have a diagnosis for ADHD (Pennington & Ozonoff, 1996; Kooijmans, Scheres, & Oosterlaan, 2000; Oosterlaan, Scheres, & Sergeant, 2005). Interestingly, studies on children with CD or ODD have shown impairments on tasks involving motivational processes such as rewards. For example, Fairchild et al. (2009) showed that both child onset and adolescent onset CD showed impairments on a hot decision making task (i.e. Risky Choice Task) not explained by deficits in cold EF (i.e. WCST) or intellectual ability. Notably, some of the inconsistencies in these findings are perhaps because studies have tested their samples on only a few select measures, compared small sample sizes, or differences in recruitment criteria. Taken together, these findings indicate that mental health disorders have significant implications for neurobehavioral functioning that appear to increase with severity of mental health issues.

Overall, researchers have noted that children with internalizing disorders can display difficulties in information and emotion processing, whereas children with externalizing disorders often show difficulties with EFs. Studies examining neurobehavioral profiles in children with internalizing or externalizing mental health psychopathology have found that children with either internalizing or externalizing mental health issues display a unique pattern of impairments on measures of EF, whereas children with both show global impairments across a variety of EF measures (Brunnekreef et al., 2007; Kusche, Cook, & Greenberg, 1993). Similarly, several researchers have examined the impact of mental health co-morbidity in childhood disorders. For example, in ADHD the presence of mental health co-morbidity reportedly interferes with EF abilities (e.g. Jarrett & Ollendick, 2008; Mattis et al., 2011; Sorenson, Plessen, Nicholas, &

Lundervold, 2011; Schatz & Rostain, 2006) and some EF impairments are associated with specific externalizing/internalizing mental health symptomology (Jonsdottir et al., 2006; Brocki & Bohlin, 2006; Di Trani et al., 2011; Graziano, McNamara, Geffken, & Reid, 2011). Therefore, the presence of co-morbidity may modulate or interacts with the executive profile of children with childhood disorders. Most studies examining neurobehavioral profiles in children with mental health co-morbidity suggest that co-morbidity likely has an impact upon functional outcomes that may have unique clinical needs. Hence, examining co-morbid groups may provide a useful approach in refining neurobehavioral profiles.

Atypical Neurodevelopment in Fetal Alcohol Spectrum Disorder (FASD)

Brain and neurobehavior. *Brief overview of FASD*. Children with FASD present with physical, emotional, mental, behavioral, and/or cognitive deficits as a consequence of prenatal alcohol exposure (PAE). FASD is a non-diagnostic umbrella term used to refer to all diagnoses and clinical presentations arising from PAE (Chudley et al., 2005). FASD diagnosis described by Astley (2004) includes four diagnostic categories: Fetal Alcohol Syndrome (FAS), partial FAS (pFAS), neurobehavioral disorder: alcohol exposed, static encephalopathy: alcohol exposed. The diagnosis of FAS requires the presence of three distinct criteria: 1) a specific pattern of facial anomalies; 2) prenatal and/or postnatal growth deficiency; and 3) some evidence of nervous system dysfunction (Clarren & Smith, 1978; Sokol & Clarren, 1989). Other terms (i.e. pFAS, neurobehavioral disorder: alcohol exposed, static encephalopathy: alcohol exposed) are used to refer to those who lack some or all of the physical features but still show neurobehavioral deficits. Notably, PAE is not the only risk factor as many of these children also have histories of prenatal (genetic conditions and poor prenatal care) and postnatal (multiple placements, adverse life experiences, and premature birth) issues that are considered in making a differential

diagnosis or to identify co-morbid diagnoses (Benz, Rasmussen, & Andrew, 2009).

A serious and debilitating outcome caused by PAE is the damage incurred to the CNS (Riley & McGee, 2005) that can manifest in a range of neuropsychological, behavioral, and neurological deficits as well as permanent damage to the brain (see Mattson, Fryer, McGee, & Riley, 2008). Studies that have compared children with FAS to alcohol-exposed children without FAS have found similar neurobehavioral deficits and no meaningful differences between these children (Mattson, Riley, Gramling, Delis, & Jones, 1997; Mattson, Riley, Gramling, Delis, & Jones, 1998; Sampson, Streissguth, Brookstein, & Barr, 2000). Hence, children affected by PAE represent significant neurobehavioral deficits regardless of the facial phenotype (Mattson, et al., 1997; Mattson, et al., 1998; Streissguth et al., 1991). The neurobehavioral deficits experienced by children with FASD have far greater functional implications and impact daily living tremendously (Streissguth & O'Malley, 2000). Furthermore, it is imperative that the initial diagnosis and co-morbidities are confirmed as early as possible, since early diagnosis and access to appropriate interventions are protective factors associated with relatively better outcomes (Streissguth et al., 2004). In response to the needs of these children, there has been a shift toward refining the neurobehavioral profile for FASD, therefore extensive research has focused on defining the specificity of these neurobehavioral deficits through comparing children with FASD to other clinical populations, and non-alcohol exposed children respectively.

Developing brain and prenatal alcohol exposure. In utero exposure to alcohol is considered one of the most common substances to affect the developing brain (Guerri, Bazinet, & Riley, 2009). The first identification of PAE adverse effects was based on autopsy findings noting a specific pattern of birth defects occurring in offspring of alcoholic mothers denoted Fetal Alcohol Syndrome (FAS; Jones, Smith, Ulleland, & Streissguth, 1973). These reports

indicated that PAE causes extensive and diffuse damage to the brain such as overall decrease in brain size and specific anomalies to corpus callosum, ventricles, cerebellum etc. (Jones & Smith, 1973), as well as specific craniofacial dysmorphism including microcephaly, short palpebral fissures, thin philtrum, a thin upper vermilion border, and growth deficiencies (Clarren & Smith, 1978). Subsequent studies confirmed that the effects of PAE occur on a continuum with FAS and prenatal death at one end and Alcohol Related Neurodevelopmental Disorders (ARND) with associated cognitive and neuropsychological deficits at the other (Mattson & Riley, 1998).

Many of the CNS effects of alcohol during prenatal and postnatal development have been confirmed using animal studies (Guerri, 2002; Hannigan, 1996). Animals exposed to ethanol (alcohol) during gestation show similar patterns of physical anomalies, growth restriction, and neurobehavioral (behavioral and learning) deficits (Barron & Riley, 1992; Weinberg, 1989). Notably, in ethanol-exposed rodents the salient craniofacial features (physical) only develop if exposure to ethanol occurs during days 7-9, which roughly corresponds to days 19-21 in humans (Sulik, 2005), whereas damage to the brain can occur throughout pregnancy. Hence, the most common and devastating consequences of PAE are the neurobehavioral outcomes. However, several factors are known to influence the effects of PAE that include the dose of alcohol and exposure pattern, timing of the exposure, genetic background of the birth mother and fetus, prenatal care, maternal age, socioeconomic (SES) status, and interactions with other substances (Guerri et al., 2009). Consequently, abstinence during pregnancy is the only way to prevent any adverse effects caused by PAE (Chudley et al., 2005).

FASD and brain-behavior relationships. Neurobehavioral findings from human studies show that PAE can lead to a range of effects involving impairments in general intellectual abilities, attention and information processing, EF, language, visual-spatial, learning and

memory, social cognition, number processing (Kodituwakku, 2009), learning difficulties, motor function, adaptive abilities, social skills, behavioral difficulties, and psychopathology (Mattson, Crocker, & Nguyen, 2011). These impairments do not appear to depend upon general intellectual functioning (Quattlebaum & O'Connor, 2012; Vaurio, Riley, & Mattson, 2011; Kerns, Audrey, Mateer, & Streissguth, 1997) and consistent evidence has reported varying general intellectual abilities ranging between very low scores within the intellectually disabled range to above average abilities (Mattson et al., 2011; Mattson & Riley, 1998).

Many of these impairments confer with brain abnormalities found in structural imaging studies of children with FASD (Lebel, Roussotte, & Sowell, 2011; Guerri et al., 2009; Wozniak & Muetzel, 2011), including studies relating deficits on cognitive and neuropsychological tasks to specific brain abnormalities (Lebel et al., 2011). Similar to autopsy findings, children with FASD show overall reductions in brain volume (Archibald et al., 2001). However, these decreases do not appear to be uniform rather the parietal lobes (Archibald et al., 2001; Sowell et al., 2002) and frontal lobes (Sowell et al., 2002) are disproportionately reduced as compared to other lobes of the brain (Mattson et al., 2008; Wozniak et al., 2009). Moreover, children with FASD show irregularities within the corpus callosum (Brookstein et al., 2007; Brookstein et al., 2002; Ma et al., 2006; Riley et al., 1995) and likely contribute to less developed neurobehavioral abilities such as attention (Coles, Platzman, Lynch, & Freides, 2002), verbal learning (Sowell et al., 2002), EF (Kodituwakku et al., 2001; Brookstein, Streissguth, Sampson, Connor, & Barr, 2002) and inter-hemispheric transfer of information (Roebuck, Mattson, & Riley, 2002; Wozniak et al., 2011). Abnormalities to subcortical regions have also been reported in children with FASD particularly the cerebellum that has been implicated in poor execution of motor function, attention, verbal learning, and classical conditioning abilities (Mattson et al., 2008). Notably,

reductions in the basal ganglia and specifically the caudate have been noted and likely compromise communication via extensive connections with the frontal lobes along the frontal-subcortical circuitry (Mattson et al., 1996).

FASD and frontal cortex. Although such findings have not exclusively focused on the frontal lobes, many of these abnormalities relate to EF deficits. EF impairments are considered the most problematic neurobehavioral deficit observed in this population (Rasmussen, 2005). Frontal lobes have been consistently reported as reduced in size and volume as well as additional cortical thickness (Lebel et al., 2011). EF deficits on neuropsychological measures have been most prominently linked to changes in corpus callosum thickening (Sowell et al., 2008). EF impairments have further been correlated with frontal lobe damage in children with FASD. For example, functional imaging studies examining task dependent regional brain changes have observed increased frontal activation during inhibitory tasks (Fryer et al., 2007a), and verbal memory tasks (Sowell et al., 2007). However, the most compelling evidence for EF deficits has been documented through behavioral studies employing neuropsychological measures to assess EF abilities across different developmental ages.

FASD and executive functions. ***EF deficits in early childhood***. As noted earlier, attention, working memory, and inhibition develop early on (Zelazo & Muller, 2002). Many of the earlier studies examining EF impairments in young children with PAE attempted to establish a direct relationship between PAE and neurobehavioral effects. Sustained attention deficits measured on the Continuous Performance Task (CPT) have been documented in children with PAE as young as 4 years of age (Streissguth, Barr, & Martin, 1984; Boyd, Ernhart, Greene, Sokol, & Martier, 1991; Brown et al., 1990). However, the relationship between PAE and sustained attention has been inconsistent, presumably because impairments in attention are

compounded by other factors such as co-morbidity with ADHD (Brown et al., 1990) and/or home environment factors (Boyd, Ernhart, Greene, Sokol, & Martier, 1991). Noland et al. (2003) compared EF abilities among a cohort (*n*=316) of preschoolers with PAE or prenatal drug exposure (cocaine or marijuana). Their findings revealed a significant negative relationship between PAE and inhibition and this effect remained even after they partialled out history of prenatal drug exposure, postnatal environment, and verbal IQ. More recently, Chiodo et al. (2009) examined the relationship between PAE and EF deficits in a cohort (*n*=75) of preschool age children. Their findings revealed that PAE was related to complex and simple test of intellectual abilities, working memory, divided attention, but not visual memory and sustained attention. However, such research emphasizes the need for more research on EF development during preschool years (Rasmussen, 2005) and have been to date limited because of the scarcity of measures available for younger children that have only recently become available (Espy, Kaufmann, Glisky, & McDiarmid, 2001).

EF deficits in children and adolescents. EF impairments have been denoted as a cardinal deficit in FASD (Rasmussen, 2005). EFs in children and adolescents are understood to involve three dissociable core constructs that include inhibition, working memory, and cognitive flexibility (Garon, Bryson, & Smith, 1998; Miyake et al., 2000), and important to goal-direct behavior such as planning, problem solving (Diamond, 2002). Various measures have been used to document the breath of EF impairments in children and adolescents with FASD (Mattson et al., 2011; Kodituwakku, 2009; Rasmussen, 2005). This section presents research on performance of children and adolescents with FASD on tests assessing inhibition, working memory, and cognitive flexibility.

Inhibition. Some studies have reported that children with FASD show deficits on

measures of inhibitory control and response inhibition processing (Mattson et al., 1999; Rasmussen et al., 2012). For example, researchers using the D-KEF's version of the Stroop task to assess inhibitory control have shown that children with FASD make significantly more errors, as compared to controls, particularly on switching and inference conditions (Mattson, Goodman, Caine, Delis, & Riley, 1999). Similarly, researchers using the go-no-go paradigm to assess the ability to inhibit a response (in conjunction with event related potentials) have found that children with FASD show poorer control relative to control children (Burden et al., 2010; Kooistra, Crawford, Gibbard, Ramage, & Kaplan, 2010). Rasmussen et al. (2013) examined attention and EF in children with FASD (age 7 to 16 years n = 32) and marked difficulties inhibiting previous responses on both the auditory attention/response set and inhibition-switching subtests of the NEPSY-II.

Working Memory. As mentioned earlier, working memory and inhibition may be important to EF performance in later childhood (Diamond, 2002; Zelazo et al., 2008). Sufficient research indicates that children with FASD show difficulties in holding and manipulating information in phonological working memory (e.g. Carmichael Olson et al., 1997). For example, Aragon et al. (2008) assessed phonological working memory in 24 children with FASD (age 7-17 years) as compared to controls. Their findings revealed that children with FASD recall fewer digits on the forward and backward digit span task as compared to control children (Aragon et al., 2008). These results are consistent with findings reported in other studies (Carmichael Olson et al., 1997; Kodituwakku, Handmaker, Cutler, Wethersby, & Handmaker, 1995; O'Hare et al., 2009). Similarly, it would appear that impairments on the digit-span tasks directly correlate with PAE (Argon et al., 2008; Carmichael Olson et al., 1997; O'Hare et al., 2009; Streissguth, Barr, & Sampson, 1990). Notably, children with FASD also show difficulties on the California Verbal

Learning Test for Children (CVLT-C) used to assess verbal learning and memory (Mattson et al., 2011). In particular, children with FASD learn fewer words even after repeated exposure (Crocker, Vaurio, Riley, & Mattson, 2011; Mattson et al., 1996). Impairments in working memory processes have been shown to interfere with other abilities in children with FASD including math (Rasmussen & Bisanz, 2011) and likely have implications for the development of other executive control and attention skills (Burden, Jacobson, Sokol, & Jacobson, 2005; Kodituwakku et al., 1995).

Set-shifting (cognitive flexibility). Numerous studies have shown that children with FASD exhibit difficulties in performing various tasks used to assess set shifting (e.g. Carmichael-Olson et al., 1997; Coles et al., 1997; Kodituwakku, et al., 1995; McGee, Schonfeld, Roebuck-Spencer, Riley, & Mattson, 2008a; Rasmussen & Bisanz, 2009; Rasmussen et al., 2013; Vaurio, Riley, & Mattson, 2008). For example, the WCST is a decision making task used to assess abstract reasoning and ability to shift concepts in response to feedback requiring hypothesis testing, inhibition, and impulse control in addition to set shifting abilities (WCST, Grant & Berg, 1948). A study by Kodituwakku et al. (1995) using the WCST to assess set shifting found that children with FASD (aged 9 to 10 years, $n = 10$) performed poorly making more errors and completing fewer categories as compared to controls. Other studies have reported similar findings (Carmichael-Olson et al., 1997; Kodituwakku et al., 2001; Vaurio et al., 2008). Similarly, McGee et al. (2008a) assessed cognitive flexibility using the Card Sort Task of the Delis-Kaplan Executive Functioning System (D-KEFS) and reported that children with FASD (aged 8 to 18 years) completed fewer sorts as compared to control children. Rasmussen and Bisanz (2009) reported that children with FASD (aged 8 to 16 years) performed significantly below the normative mean of 10 on the D-KEFS Card Sort Task. More recently, Rasmussen, Tamana, et al.

(2013) tested set-shifting and concept formation using the Animal Sort Task of the NEPSY-II and reported that children with FASD (aged 7 to 16 years) performed significantly poorer than control children. Taken together, difficulties in set-shifting and cognitive flexibility and abstract reasoning indicate that children with FASD possess impaired problem-solving abilities.

Other areas of neurobehavioral functioning. *Face and emotion processing*. Face memory deficits have been inconsistently reported in children with FASD. Some studies have found impairments on face recognition tasks (Wheeler, Stevens, Sheard, & Rovet, 2012; Rasmussen, Horne, & Witol, 2006) whereas other studies have reported no significant impairment in comparison to age-relevant norms (Autti-Ramo et al., 2002; Pei, Rinaldi, Rasmussen, Massey, & Massey, 2008) and typically developing controls (Uecker & Nadel, 1996). Furthermore, using tasks to test identification of emotions in faces (e.g. DANVA, Minnesota Test of Affective Recognition, Florida Affect Battery) researchers have found that children with FASD exhibit deficits in face emotion processing (Greenbaum, Stevens, Nash, Koren, & Rivet, 2009; Kerns et al., 2015).

Adaptive Abilities. Researchers have consistently reported poor adaptive abilities in children with FASD, which are important for daily and independent function. Children with FASD show adaptive deficits in the domains of communication, daily living skills, and socialization (e.g. Crocker Vaurio, Riley, & Mattson, 2009; Whaley, O'Connor, & Gunderson, 2001) that appear to worsen with age (Crocker et al., 2009) as reported on the Vineland Adaptive Behavior Scales (parent-rated version). Notably, deficits in adaptive functioning correlate with EF deficits on neuropsychological (Ware et al., 2012a) and behavioral measures (e.g. BRIEF; Denys, Zwaigenbaum, Andrew, Tough, & Rasmussen, 2011) as well as with difficulties in social problem solving (McGee, Fryer, Bjorkquist, Mattson, & Riley, 2008b). Therefore, it is likely that

adaptive function deficits relate to other adverse outcomes such as externalizing and/or internalizing mental health problems.

Executive function behaviors. Several studies have reported on EF behaviors in home environments using parent report measures of EF behaviors (measured on the Behavior Rating Inventory of Executive Functioning; BRIEF). Studies have reported that children with FASD display significant impairments on measures of EF behaviors as compared to age adjusted norms (Rasmussen, et al., 2006; Rasmussen, McAuley, & Andrew, 2007) and age matched controls (Schonfeld, Paley, Frankel, & O'Connor, 2006). Furthermore, these deficits appear to worsen with age relative to the norm (Rasmussen et al., 2007) and relate to other areas of functioning such as poorer social skills, increased problem behaviors (Schonfeld et al., 2006), and poor adaptive abilities (Denys et al., 2011).

Neurobehavioral Profile. Despite extensive research, a neurobehavioral profile for FASD remains elusive (Kodituwakku, 2009). In a recent review, Mattson et al. (2011) conferred that the neurobehavioral profile for children with FASD includes impairments in many areas previously reported by Kodituwakku (2009) involving IQ, EF, memory, language, motor function, academic, adaptive skills, social skills but additionally highlighted that behavioral and psychiatric issues are considered as part of the neurobehavioral phenotype of FASD. In general, children with FASD show marked difficulties on neuropsychological measures that involve more complex processing and place greater demands on EFs (Mattson et al., 2011; Kodituwakku, 2009). Some studies have also observed age-related differences on tasks of EF (Rasmussen & Bisanz, 2009; Tamana et al., 2012), which may relate to some of the adverse outcomes that can emerge including persistent internalizing and externalizing psychopathology (Streissguth, Barr, Brooktein, Sampson, & Carmichael-Olson, 1999).

Mental Health Co-morbidity in FASD

Prevalence of Mental Health Issues. A high number of children with FASD have been described as having mental health problems (Pei et al., 2011). The estimated prevalence rates for mental health disorders and issues in individuals with FASD are disproportionately high as compared to the general population (Pei et al., 2011). In a review paper, Pei, et al. (2011) reported a high prevalence of mental health issues in 90% of individuals with FASD and PAE. In a recent paper reporting on the prevalence of mental health issues among children and adolescents with FASD or PAE, it was found that up to 94.2% of children had a mental health diagnosis (Chasnoff et al., 2015). Although there are no known statistics for Canada, Canadian children with FASD are reportedly at high risk for persistent mental health problems (Rasmussen, Kulley-Martens, Cui, Tough, Zwaigenbaum, & Tough, 2013). Noticeably, both externalizing mental health disorders such as ADHD, CD, and internalizing mental health disorders such as anxiety, depression, and mood are reportedly some of the most prevalent co-morbidities in this population (Pei et al., 2011).

PAE is related to significant psychosocial impairment in number of domains (Roebuck, Mattson, & Riley, 1999). Mattson and Riley (2000) noted that 90.1% of children with PAE exhibited internalized and externalized problems that fell within the clinically significant range; this was found to be disproportionately greater for externalized behaviors although many internalized behaviors were also elevated as compared to a typically developing children. O'Connor et al. (2002) reported that 87% of sample of individuals with PAE met criteria for a psychiatric disorder that represented mood disorder, bipolar disorder, and major depression. Fryer et al. (2007) found that 97.44% of their sample of individuals with PAE met criteria for an Axis 1 disorder that represented ADHD, Depression, ODD, CD, and phobia. Similarly, Burd et

al. (2003) noted a range of co-morbidities in their sample with ODD and mood disorders among the highest, and the distribution of co-morbidities appeared to depend upon the severity of FASD diagnosis. Furthermore, Astley, (2010) observed that 75% of their clinically referred sample had received a diagnosis for one or more mental health co-morbidity. Rasmussen et al. (2013) found in a Canadian sample of children with FASD (n=46) and PAE (n=26) that 87% of children with FASD and 76% of children with PAE exhibited a mental health co-morbidity with the most common being ADHD, ODD, depression, anxiety, and reactive attachment disorder respectfully. Moreover, Ware et al. (2012b) found that children with heavy PAE exhibit similar rates for internalizing mental health disorders such as MDD and GAD to children with heavy PAE/ADHD; however, externalizing mental health disorders (i.e. CD and ODD) were significantly higher in children with heavy PAE/ADHD than children with heavy PAE only (Ware et al., 2012b).

Children with FASD appear to be at increased risk for co-morbid disorders (Streissguth & O'Malley, 2000; Steinhausen & Spohr, 1998) and poor outcomes in terms of mental health have been well documented in FASD. These mental health issues appear to persist and potentially worsen with age (Steinhausen & Spohr, 1998) or lead to more severe mental health psychopathology in later life (Pei et al., 2011; Painter et al., 2010). Notably, children with FASD are frequently diagnosed with one or more co-morbid mental health disorder (Burd et al., 2003; Paintner et al., 2012). Hence, risk for co-morbid mental health disorders is increased among children with FASD (Paintner et al., 2012). Notably, Paintner et al. (2012) model of co-morbidity in FASD infers that individuals with FASD show increase severity or complexity of co-morbid disorders because of causal factors (e.g. intellectual disability) and lower threshold for expression of genetic or environmental liability (e.g. speech language disorder).

Stress-Diathesis Hypothesis in FASD. As mentioned earlier, the Diathesis-Stress model in mental health infers that individual's exposed to multiple stresses over the lifetime are at increased risk for developing a mental health disorder (Ingram & Luxton, 2005; Zuckerman, 1999). In line with this theory, the Stress-Diathesis hypothesis in FASD suggests that exposure to multiple stressors over a time period can lead to vulnerability for developing psychopathology due to an alcohol-induced predisposition. Hence, PAE may lower threshold against genetic and/or environmental influences (Paintner et al., 2012). There has been some support for the Stress-Diathesis hypothesis in the FASD literature particularly in relation to prevalence and risk for anxiety and depression in individuals with FASD (Hellemans, Sliwowska, Verma, & Weinberg, 2010). The hypothalamic-pituitary-adrenal (HPA) axis has an important role in depression and anxiety (Gutman & Nemeroff, 2003). Studies have shown that PAE induces changes in the HPA function that parallel changes in depressed individuals (e.g. Van Waes et al., 2010; Hellemans et al., 2010) and can alter response to mild or chronic stress (Hannigan, 1996 for a review). Hellemans et al. (2010) propose that long-term changes in HPA axis caused by PAE increases sensitivity to adverse environmental stressors, thus heightens susceptibility for developing anxiety or depressive disorders. Hence, PAE may act as a precursor to pathological changes such as a sensitized HPA axis that predispose children with FASD to developing internalizing co-morbidities. For example, Hellemans, et al. (2008) found that in adult rodents exposed to a both PAE and chronic mild stress show greater anxious and depressive symptoms than adult rodents exposed to either one alone. They proposed that these data provide support for HPA axis dysfunction as likely an underlying factor for anxiety and depressive symptoms among with histories of PAE (Hellemans, Sliwoska, Verma, & Weinberg, 2008). Of note, the HPA axis has been implicated as a risk marker for cognitive deficits particularly memory and selective

attention (Lupien et al., 1994) and perhaps for children with FASD some of the neuropsychological impairments are exacerbated by the presence of co-morbid depression or anxiety. Hence, for children with FASD an increased vulnerability to life and developmental stressors appear to be inherent.

Risk and protective factors in FASD in relation to mental health. PAE is clearly a biological risk factor for poor mental health outcomes (i.e. Sood et al., 2001; Sayal, 2007; Sayal et al., 2009; Sayal, Heron, Golding, & Emond, 2007). However, the findings of prospective birth cohort studies have revealed mixed results about the direct relationship between PAE and mental health problems in later childhood. Some studies have reported that both low and high levels of PAE correlate with externalizing mental health problems such as hyperactivity and inattention even after controlling for other risk factors (i.e. maternal education, maternal age, parity, other exposures, maternal mental health, relationship status, birth weight, gestational age) (Disney, Iacono, McGue, & Legrand, 2008; D'Onofrio et al., 2007; Larkby et al., 2011; Sayal, 2007; Sayal et al., 2007). Other studies have found that the relationship between PAE and mental health issues is mediated by other factors such as other prenatal exposures or adverse postnatal environment (O'Connor & Paley, 2006; Robinson et al., 2010; Rodriguez et al., 2009). Therefore, it would appear that PAE likely increases vulnerability to prenatal and postnatal risk factors, thereby leading to mental health problems.

Currently, there exists limited evidence depicting the prevalence of risk and protective factors in this vulnerable population. Relatively few studies have profiled risk and protective factors during pregnancy, at birth, and postnatal period. The following sections will report on prenatal and postnatal risk factors reported in this population and the implications for mental health outcomes.

Prenatal risk factors. Flynn et al. (2009) found that among those women who reported alcohol-use at pre-pregnancy had poorer obstetrical outcomes including preterm rupture membranes, fewer gestation weeks, and decreased birth weight. However, it is not clear from this study whether alcohol use at pre-conception or during pregnancy related to obstetrical outcomes. In a case-control study, Coyne et al. (2008) examined obstetrical outcomes for mothers of children subsequently diagnosed with FAS as compared to non-exposed controls and found higher parity, fewer antenatal visits, and higher number of antenatal and delivery complications. In contrast, Astley et al. (2010) conducted a retrospective clinical file review of children seen by an FASD Clinic and found that mothers of children with FASD frequently reported poorer prenatal care (i.e. poor nutrition, fewer antennal visits) and prenatal exposure to illicit substances, and this did not significantly differ according to FASD diagnostic group. However, it is important to note that these findings are difficult to generalize to the entire spectrum or to ascertain whether similar rates would occur in mothers of all children born with an FASD and PAE. Hence, further studies are required to replicate these results by comparing prenatal histories of mothers who have given birth to children with FASD or PAE.

Postnatal risk factors. In a study by Streissguth et al. (2004), they followed a birth cohort with PAE (aged 6-21 years) and found that specific risk and protective factors were related to adverse and relatively positive outcomes in their sample, including mental health. *Protective factors* associated with relatively better outcomes included early diagnosis, stable home/nurturing environment, and limited exposure to adverse life experiences such as frequent foster placement, multiple caregiving placement, exposure to violence, instability, neglect, abandonment, and emotional or physical abuse (Streissguth, et al., 2004). Notably, having intellectual abilities above 70 and a diagnosis for FAS or FAE were identified *risk factors* in

their sample. Rasmussen et al. (2013) documented similar rates of early life adversities that represented the type of living arrangement, multiple caregiving placements, frequent foster placement, living in a poor quality home, and exposure to abuse, neglect, or violence. Astley et al. (2010) et al. in addition to identifying prenatal risk factors (reported earlier) they found a high prevalence of postnatal risk factors that involved substance use in postnatal environment, multiple placements, and physical/sexual abuse. Notably, 70% of their sample had a co-morbid diagnosis for a mental health disorder; however, the contribution of risk and protective factors to these high rates was not explored in this study. This means that many children with FASD experience 'double jeopardy' because of they also experience adverse childhood experiences and poor caregiving environments (Carmichael-Olson, Rosalind, Gelo, & Beck, 2009).

Studies examining the postnatal environment have also documented an association between postnatal risk and protective factors and mental health outcomes for children with FASD. Kopen et al. (2009) found that for children with FASD having a stable caregiving environment during the first 5 years of life had a strong effect of emotional and behavioral control. O'Connor & Kasari's (2000) study of 41 mothers and their children with PAE found a relation between maternal depression and child depressive symptoms. Interestingly, PAE was reportedly the strongest factor mediating this relationship and not mother-child interaction, which implies that perhaps PAE alters a child's ability to respond to the external environment making it difficult to overcome depressive symptoms (O'Connor & Kasari, 2000). Similarly, Walthall et al. (2008) reported that adolescents with FASD living in a single/divorced or a non-biological home had higher rates of psychopathological disorders as compared to adolescents with FASD living in a stable home or with a biological caregiver. Furthermore, although limited research has addressed the impact of trauma, in a study by Henry, et al. (2007) they found that

children with FASD and trauma had poorer neurobehavioral outcomes than children with trauma only. Other studies have reported on the relation between risk and protective factors and behavioral/emotional issues measured on standardized rating scales (e.g. CBCL, BASC-2 etc.). Fagerlund et al. (2011) examined the relationship between risk and protective factors and behavioral problems in 73 children with and without FAS. They found that length of time spent in residential care was associated with externalizing and internalizing mental health issues. Notably, children without FAS appeared to be at greater risk for mental health issues particularly in the internalizing domain. However, their study was limited because they were only able to explore risk and protective factors in relation to diagnosis, living situation, and school remedial help and rates of mental health co-morbidity were unknown. More recently, Rasmussen, et al. (2013) examined mental health problems in relation to postnatal risk/protective factors in a sample of 72 children with PAE and FASD. They found that age at FASD assessment was associated with both internalizing and externalizing issues, thus confirms that the child's age at FASD assessment or diagnosis is an important protective factor against mental health co-morbidity as reported in previous research (Streissguth et al., 2004). In addition, parental medication use was also associated with internalizing issues and suggests that perhaps parental health is an important risk factor for developing anxiety and depression in children with FASD (Rasmussen et al., 2013).

Limitations. Studies of risk and protective factors in FASD indicate that identification of specific factors may be critical in considering mental health care for children with FASD. Although there has been some research completed in this area, very little research has examined risk and protective factors mediating mental health issues in this population. Findings from these studies indicate that environmental factors may influence adverse outcomes (including mental

health) in FASD (Streissguth et al., 2004; Fagerlund et al., 2010). In particular, early diagnosis is important in reducing risk for poor outcomes related to mental health (Rasmussen et al., 2013; Fagerlund et al., 2010; Streissguth et al., 2004). However, research on risk and protective factors during pregnancy, at birth, *in addition* to family history, parental mental health, and postnatal environment associated with mental health diagnoses in FASD is lacking. Further research using larger datasets and multiple risk and protective factors to explore more specifically the relation between these factors and different types of persistent and/or severe mental health co-morbidities in FASD is needed.

Neurobehavioral functioning in FASD with mental health co-morbidity. The high prevalence of co-morbid disorders in children with FASD may be that these issues relate to severity of the neurobehavioral deficits observed in these children. There is some evidence that children with FASD and PAE with lower intellectual abilities are at increased risk for mental health co-morbidities (Sophr, Willms, & Steinhausen, 1993; Steinhausen & Spohr, 1998; Streissguth et al., 1999; Walthall, O'Connor, & Paley, 2008). However, not all studies have reported a relationship between lower intellectual abilities and mental health co-morbidities in individuals with FASD (Streissguth et al., 2004; Roebuck et al., 1999). Importantly, IQ is not reflective of function as many children with FASD show scores within the normal range but still exhibit impairments in some neurobehavioral domains particularly those involving EF, verbal processing, and working memory (Vaurio et al., 2011; Mattson, et al., 2011; Mattson & Riley, 2000; Mattson, Goodman, Caine, Delis, & Riley, 1999). Despite the identified higher rates of several co-morbid mental health disorders in children with FASD there is limited research examining how neurobehavioral impairments beyond IQ relate to co-morbid mental health issues in children with FASD. To date, most research has focused on the neurobehavioral profile of

children with FASD in comparison to children with FASD and/or ADHD.

Attention deficit hyperactivity disorder (ADHD). ADHD is a behavioral disorder characterized by poor sustained attention, impulsiveness, and hyperactivity (APA: American, 2013) and is considered one of the most prevalent childhood disorders, affecting 5% of children (APA, 2013). These behavioral deficits arise in early childhood, typically before age 7 years, and persist over development (Barkley, 2002; Barkley, 1997). The etiological cause for ADHD has been highly implicated in genetics (Eaves, Silberg, & Meyer, 1997) but there is increasing recognition of other etiological causes of ADHD, in particular PAE (O'Malley & Nanson, 2000).

Neurobehavioral comparisons of FASD and ADHD. ADHD is the most frequently reported co-morbidity in children with FASD (Fryer, McGee, Matt, Riley, & Mattson, 2007b). Notably, many children with FASD may still display ADHD type symptoms even without an ADHD diagnosis. Despite the potential overlap in etiology between these disorders, several studies have shown that children with FASD can be differentiated from children with ADHD regardless of manifestation of clinically similar behavior (Mattson, Crocker, Nguyen, 2011).

Studies comparing children with FASD to ADHD indicate that the two disorders are distinct in a number of neurobehavioral domains involving problem solving, verbal fluency, shifting attention, verbal encoding, daily living skills, face and emotional processing (see Mattson et al., 2011 for a review) as well as adaptive functions (Crocker et al., 2009; Ware et al., 2012a) and psychopathology (Ware, et al., 2012b). In particular, children with FASD are significantly more impaired on measures of EF involving cognitive flexibility and verbal fluency as compared to children with ADHD (Vaurio et al., 2008). Similarly, children with FASD show greater difficulty on tasks of shifting attention, encoding information, and problem solving than children with ADHD (Coles et al., 1997). Other areas involving adaptive functions have also

been found to differ between children with FASD and ADHD. For example, Crocker et al. (2009) found that children with FASD show greater impairments in adaptive abilities as compared to ADHD. Furthermore, EF has been associated with both FASD and ADHD as an underlying cause for adaptive functions (Ware et al., 2012a). However, in children with FASD deficits in adaptive functions more specifically correlate with non-verbal EF measures (Ware et al., 2012a). More recently, Mattson et al. (2012) using latent profile analysis found that children with heavy PAE were distinguishable from children with ADHD on measures of EF, spatial working memory, and delayed matching, which further substantiates similar results indicating group differences on measures of EF (Mattson et al., 2011).

Furthermore, Rasmussen et al. (2010) compared children with FASD (aged 5-17 years) with and without an ADHD co-morbidity across several neurobehavioral domains. They found no significant difference between children with FASD and FASD/ADHD on any neurobehavioral domain besides attention suggesting that having a diagnosis for ADHD co-morbidity had little effect on the neurobehavioral profile. However, one limitation noted may be that they were unable to compare group differences on specific neurobehavioral measures thus warrants further investigation. Similarly, using the NEPSY-II, Rasmussen, Tamana et al. (2012) reported no significant differences between children with FASD and FASD/ADHD across several neurobehavioral domains (including EF and attention). Furthermore, Crocker et al. (2011) found that relative to children with ADHD, children with FASD/ADHD performed significantly worse on a measure of verbal learning and memory (i.e. California Verbal Learning Test for Children), specifically the learning trials and recognition subtests.

Other studies have begun to examine the within FASD profile by comparing the profile of children with FASD with and without ADHD co-morbidity. Raldiris et al. (2014) compared

the cognitive and behavioral performance of four groups of children and adolescents (aged 6 to 16 years) with FASD, ADHD, FASD + ADHD, and other neuropsychological disorders. Their findings revealed the FASD group performed significant worse on measures of intellectual ability, perceptual reasoning, verbal comprehension, working memory (measured by the WISC-IV), and externalizing problems (measured by the BASC-2), as compared to the ADHD group. The FASD + ADHD group showed a similar profile but performed significantly worse than the ADHD group on the verbal comprehension measure and displayed higher levels of hyperactivity and withdrawal. These results confirm previous work indicating that children and adolescents with FASD show significant impairments compared to children and adolescents with ADHD. Similarly, Boseck et al (2014) compared the cognitive and adaptive abilities in a sample of children and adolescence (mean age 10 years) with FASD and ADHD co-morbidity as compared to those with ADHD but not prenatal alcohol exposure. Their findings revealed that children with FASD + ADHD performed significantly worse on measures of verbal ability, perceptual reasoning, working memory, processing speed, and overall adaptive skills.

Limitations. Previous research has extensively studied the neurobehavioral profile in children with FASD and/or ADHD as compared to children with ADHD. These findings indicate that children with FASD/ADHD show a unique pattern of deficits that can be differentiated from children with ADHD. However, the same understanding of how other types of mental health co-morbidity present in FASD has not been researched. Therefore, the relationship between neurobehavioral function and other common mental health co-morbidities and consequential treatment needs are lacking. It cannot be assumed that other co-morbid disorders will have the same impact on function as in previous research. Hence, there is a need to look beyond ADHD. Studies that represent co-morbidity with other mental health disorders found in this population

are required and are critical to informing the etiology of PAE in mental health and developing effective mental health screening and treatments.

Introduction to thesis research

In an attempt to extend previous research this project explored the nature of mental health co-morbidity in children and adolescents within the context of FASD. The FASD literature suggests an association between biological and environmental risk factors and the development of a mental health disorder. However, there is currently no information on how risk factors associated with different types of mental health co-morbidity particularly within the context of FASD. Furthermore, few studies have examined the impact of mental health co-morbidity upon the functioning of children and adolescents with FASD. Thus, the goals of the current study were to examine 1) the prevalence of mental health diagnoses, 2) associated risk factors for poor mental health outcomes, and 3) the impact of having a mental health co-morbidity upon neurobehavioral functioning among children and adolescents with FASD. I investigated the mental health of children and adolescents with FASD by conducting a retrospective and a prospective follow-up study. In study 1, I explored prenatal and postnatal risk factors associated with having a mental health co-morbidity in a large retrospective sample of children and adolescents assessed for FASD. I specifically explored the hypothesis that specific prenatal and postnatal risk factors are associated with having a co-morbid internalizing or externalizing diagnosis. In study 2, I compared the neurobehavioral profile between children and adolescents with FASD/PAE, with and without mental health co-morbidity, on a variety of neurobehavioral measures largely involving executive functioning, as well as attention, emotion processing, and mental health. I expected to find that children and adolescents with both FASD/PAE and a mental health co-morbidity would display greater neurobehavioral impairments. The next two

chapters will describe the results of this work.

CHAPTER III

Prenatal and Postnatal Risk Factors for Mental Health Disorders Diagnosed in Children and Adolescents with FASD

Fetal Alcohol Spectrum Disorder (FASD) affects as many as 2 to 5 per 100 individuals in the United States and some Western European Countries (May et al., 2009). Children and adolescents with FASD present with physical, emotional, mental, behavioral, and/or cognitive deficits as a consequence of prenatal alcohol exposure (PAE). The term FASD is a non-diagnostic umbrella term used to refer to all diagnoses and clinical presentations arising from PAE (Chudley et al., 2005). The FASD diagnosis described by Astley (2004) includes four diagnostic categories: Fetal Alcohol Syndrome (FAS), partial FAS (pFAS), neurobehavioral disorder: alcohol exposed, static encephalopathy: alcohol exposed. The diagnosis of FAS requires the presence of three distinct criteria: 1) a specific pattern of facial anomalies; 2) prenatal and/or postnatal growth deficiency; and 3) some evidence of nervous system dysfunction (Clarren & Smith, 1978; Sokol & Clarren, 1989). Other terms (i.e. pFAS, neurobehavioral disorder: alcohol exposed, static encephalopathy: alcohol exposed) are used to refer to those who lack some or all of the physical features but still show neurobehavioral deficits. In addition to confirmed prenatal alcohol exposure, prenatal factors and postnatal factors are ranked as part of the diagnostic assessment using a 4-point Likert scale to describe relative risk, which ranges from 0 (unknown) to 4 (high risk), as endorsed by both the four-digit Diagnostic Code and the Canadian Guidelines. Hence, both degree of PAE and the influence of prenatal factors (genetic conditions and poor prenatal care) and postnatal factors multiple placements, adverse life experiences, and premature birth) are each considered in making a differential diagnosis and to identify a co-morbid condition (Benz et al., 2010).

The burden of mental health co-morbidities diagnosed among individuals with FASD has been consistently reported in the literature. Mental health issues are observed at exceptionally high rates among individuals with FASD, affecting over 90% of the FASD population (Pei et al., 2011), and up to 94.2% of children and adolescents with FASD or PAE (Chasnoff et al., 2015). Children and adolescents with FASD display significant mental health issues affecting both externalizing and internalizing domains (Mattson and Riley, 2000). The most common co-morbidities reported among individuals with FASD include Attention Deficit Hyperactivity Disorder (ADHD), oppositional defiant disorder, depression, anxiety, and mood disorders (Pei at al., 2011). Studies in children and adolescents born to mothers who consumed alcohol during pregnancy have described an association between PAE and behavioral difficulties (i.e. Sood et al., 2001; Sayal, 2007; Sayal et al., 2009; Sayal, Heron, Golding, & Emond, 2007). Findings from prospective birth cohort studies have revealed mixed results about the direct relationship between PAE and externalizing and internalizing mental health issues in later childhood. Some studies have reported that both low and high levels of PAE are associated with externalizing issues such as hyperactivity and inattention, even after controlling for potential confounding factors (i.e. birthing outcomes, other prenatal exposures, maternal mental health etc.) (Disney, Iacono, McGue, & Legrand, 2008; D'Onofrio et al., 2007; Larkby et al., 2011; Sayal, 2007; Sayal et al., 2007). Other studies have found that the relationship between PAE and mental health issues is mediated by other factors such as other prenatal exposures or adverse postnatal environment (O'Connor & Paley, 2006; Robinson et al., 2010; Rodriguez et al., 2009). These findings suggest that there may be a biological basis for mental health issues in the FASD population. It has been suggested that PAE likely increases vulnerability to prenatal and postnatal risk factors thereby leading to mental health problems (O'Connor, 2012).

Children and adolescents with FASD are often described as facing *double jeopardy* because in addition to their histories of PAE they also experience adverse childhood experiences and poor caregiving environments (Carmichael-Olson, Rosalind, Gelo, & Beck, 2009). Findings from Streissguth et al. (2004) study identified key risk and protective factors resulting in relatively better outcomes, including mental health issues. These factors included receiving an early FASD diagnosis, a stable home/nurturing environment, and limited exposure to adverse life experiences such as frequent foster placement, multiple caregiving placement, exposure to postnatal trauma such as violence, instability, neglect, or abuse. There is growing evidence that prenatal and postnatal risk factors can increase risk for later behavioral, emotional, or psychiatric problems. Poor mental health can have further negative impacts on an adolescent's ability to achieve in life and academically and are consequently less likely to experience positive outcomes. Extensive research has documented the prevalence of mental health prevalence issues in this population. However, there is limited research examining multiple environmental factors that may contribute to mental health outcomes diagnosed in this population.

Therefore, the purpose of this research was to examine prenatal factors (such as birth outcomes, perinatal complications, substance exposure during pregnancy) and postnatal factors (such as living situation, exposure to abuse, neglect, exposure to violence), and their association with mental health outcomes in a large sample of children and adolescents with FASD/PAE. I set out to examine three research questions. First, I described the pattern and prevalence of different types of mental health disorders diagnosed in a sample of children and adolescents with FASD/PAE. I expected to find higher rates of mental health diagnoses than reported in the general population, affecting both the externalizing and internalizing domains. Secondly, I described the types of prenatal and postnatal factors documented in the sample, and I anticipated

that higher rates of adverse factors would occur among those children and adolescents with FASD/PAE diagnosed with a mental health disorder. Finally, I examined the association between risk factors and mental health outcomes, and in particular whether experiencing more adverse events significantly increased risk for having a co-morbid internalizing or externalizing diagnosis. Prior researchers have found that the relationship between PAE and mental health issues is mediated by other prenatal exposures or adverse postnatal environmental factors (e.g. O'Connor & Paley, 2006; Robinson et al., 2010; Rodriguez et al., 2009); therefore, I expected to find a significant association between postnatal risk factors and internalizing co-morbidities, and between prenatal risk factors and externalizing co-morbidities. Identifying the role of risk factors associated with poor mental health outcomes is important for increasing resiliency among children and adolescents with FASD/PAE.

Method

Sample.

All children with FASD seen by a large FASD diagnostic clinic between 2002 and 2012 were eligible for inclusion in this study. The current study included a sample of 209/282children aged between 3 to 17 years (9.3 years, *sd* = 3.5), including children with an FASD diagnosis (n=158, 53.9% male) and those children with PAE (n = 51, 63.0% male) but did not meet diagnostic criteria for a formal FASD diagnosis were included. Sufficient data was collected for 122 children with FASD or PAE diagnosed with a mental health disorder (9.7 years, 56.9% male) and 87 children with FASD or PAE but no mental health diagnosis (8.6 years, 55.7% male), resulting in a total sample size of 209 children and adolescents. All children and adolescents will be collectively referred to as children and adolescents with FASD/PAE. See Table 1.1 for basic demographic characteristics.

Diagnostic information was obtained from clinical files. The initial FASD assessment for each child was made by a multidisciplinary team, which consisted of a developmental pediatrician, psychologist or neuropsychologist, speech pathologist, occupational therapist, and a social worker. Evaluations consisted of a full pediatric, neurologic, and dysmorphology examination, psychological testing, and speech and language and motor/sensory evaluation. Only children with confirmed prenatal alcohol exposure were seen by the FASD clinical team. FASD diagnoses were based on the 4-digit diagnostic code (Astley, 2004) and the Canadian guidelines (Chudley et al., 2005). Diagnostic information is ranked using a 4-point Likert scale to independently rank growth deficiency, facial dysmorphology, brain dysfunction, and alcohol use. Confirmation of PAE is obtained through review of prenatal history, birth documents, health records, and parental interview. To receive a diagnosis for FASD using the 4-digit diagnostic code (Astley, 2004), children also have to demonstrate deficits in three or more neurobehavioral domains that include neurological signs, sensory-motor, communication, attention, cognition, academic achievement, memory, executive function, and adaptive functioning. The term PAE refers to those children who received the diagnostic decision of neurobehavioral disorder-alcohol exposed but not FASD. To receive the diagnostic decision of PAE, children did not meet the full criteria to receive an FASD diagnosis as laid out in the 4-digit diagnostic code (Astley, 2004). A number of factors are taken into account when considering if the clinical presentation is best accounted for by underlying brain injury due to maternal alcohol consumption. Children with PAE but not formal FASD diagnosis may not have met criteria because the child did not display a pattern of neurobehavioral or physical features that are characteristic of FASD or the clinical presentation is better accounted by a genetic condition, trauma, or other neurobehavioral disorder. Alternatively, children may have received a deferred decision at the time of their

assessment due to the age of the child or other environmental factors potentially confounding clinical presentation. FASD diagnostic groups included: fetal alcohol syndrome (FASD); partial fetal alcohol syndrome (pFAS); static encephalopathy: alcohol exposed; neurobehavioral disorder: alcohol exposed; and neurobehavioral disorder: alcohol exposed not FASD (PAE).

Information on prenatal (genetic conditions, other substance exposures) and postnatal (e.g. multiple placements, abuse) factors is also ranked using the 4-digit diagnostic system at the time of each child's initial assessment. A score of 4 indicates high risk, 3 indicate some risk, 2 indicate unknown risk, and 1 indicates unremarkable risk. The FASD diagnostic process uses information about prenatal and postnatal factors to make a decision about differential or co-morbid diagnoses. All potential co-morbidities are considered by the FASD diagnostic team when making an FASD diagnosis. Mental health co-morbidities were identified at the time of the child's FASD assessment or previously by a referring community mental health program or psychiatric team. All mental health diagnoses confirmed by the FASD Clinical Team were included in this sample.

Mental health diagnoses were separated into two groups: externalizing or internalizing disorders. Inclusion criteria for externalizing mental health disorders included attention deficit-hyperactivity disorder (ADHD) and oppositional defiant disorder or conduct disorder; and for internalizing disorders included anxiety, post-traumatic stress disorder (PTSD), depression, and attachment/reactive attachment disorder.

Table 1.1

Demographic information for FASD/PAE and FASD/PAE + mental health diagnosis groups

Characteristic	FASD/PAE - no MH (*n*=87)	FASD/PAE + MH (*n*=122)	*p-value*
Age	8.6 (3-16)	9.7 (3-17)	.024[a*]
Sex % Male (n)	55.7% (54)	56.9% (70)	.854[a]
FASD Diagnosis			.031[b*]
Fetal alcohol syndrome (FAS)	0% (0)	2.3% (3)	
Partial fetal alcohol syndrome (pFAS)	1.2% (1)	6.6% (8)	
Static encephalopathy: alcohol exposed	48.2% (41)	47.5% (58)	
Neurobehavioral disorder: alcohol exposed	27.1% (23)	18.9% (23)	
Prenatal alcohol exposure (PAE): no diagnosis	24.1% (21)	24.6% (30)	
Intellectual ability			.138[a*]
High average range	0 (-)	0.8% (1)	
Average range	19.0% (15)	31.4% (37)	
Low average range	32.9% (26)	33.1% (39)	
< Intellectual disability range	48.1% (38)	34.7% (41)	
Missing	9.2% (8)	3.3% (4)	
Child sleep issues % yes (n)	11.5% (10)	31.4% (38)	.001*

[a] Data was analyzed using analysis of variance (ANOVA)
[b] Data was analyzed using chi square statistic
[c] Intellectual ability was assessed using the WISC-III or WISC-IV or WPPSI

Procedures

Retrospective data was collected based on information recorded from 282 clinical charts. No prior knowledge regarding the child's diagnosis or mental health co-morbidities was known. A sample of 209/282 charts was included in this study. Files were excluded if the child was under 3 years at the time of being seen by the FASD clinical team, the file was a second assessment, inadequate information was available, or I was unable to retrieve the main clinical chart for more detailed information. A coding form was used to gather information from clinical records to obtain basic information about FASD diagnosis, mental health co-morbidities, age, gender, IQ classification, assessment date, prenatal and postnatal information, and family history

(see Appendix A). All procedures were reviewed and approved by the Health Research Ethics Board at the University of Alberta as well as Alberta Health Services (AHS).

Data collected included information on basic demographics (i.e. age at assessment, gender, intellectual ability); diagnosis (i.e. FASD or PAE, FASD diagnosis, diagnostic code, alcohol exposure, prenatal score, postnatal score); mental health co-morbidity (confirmed by FASD team and/or previous diagnosis as made by community mental health professional); prenatal factors during pregnancy and at birth (i.e. other teratogens, prescribed medications, biological mothers education, maternal/paternal learning difficulties); postnatal factors (i.e. number of placements, multiple moves, biological mothers relationship status, abuse, abandonment, adequate stimulation, failure to thrive, exposure to caregiver drug/alcohol problem, head injury, childhood problems e.g. emotional, school, problems with sexuality); and family history (biological parents mental health, substance use problems, trouble with the law, medical diagnosis). See Appendix B for a complete list and definition for each study variable.

Data Coding *Predictors.* Child characteristics were coded for gender (0 = male, 1 = female), intellectual ability (0 = borderline to intellectual disability range, 1 = low average to high average range), FASD diagnosed (0 = PAE, 1 = FASD), child sleep issues (0 = no, 1 = yes), age (continuous score ranging from 3 to 17 years). Binary predictor variables were coded as 0 (non reported) and 1 (yes or suspected) for each prenatal and postnatal factors. Continuous predictor variables were coded as a score or on a Likert scale. See Appendix B.

ACE score. I retrospectively assigned an accumulative risk score to each child in this current study based on information collected about each child's history of adverse postnatal experiences from birth to age of FASD assessment. Information about adverse childhood experiences was obtained from clinical files as reported by caregiver, family member, and/or

social services documentation. The adverse childhood experiences (ACE) questionnaire was used to generate an accumulative risk score. Each child was assigned a score ranging from 0 to 10 based on the ACE 10 survey. ACEs were identified based on retrospective data and the number of experiences endorsed were coded and counted as any of the 10 ACE categories. Ten questions were retrospectively applied to determine whether the child had reportedly experienced physical, sexual, emotional abuse, and/or neglect, not been raised by both biological parents, or ever lived in a household with substance abuse, legal trouble, caregiver mental illness, or domestic violence (see Appendix C). ACE was coded as a score ranging from 0 to 10 and as a binary variable coded as 0 (ACEs endorsed = 1 to 3) and 1 (ACEs endorsed = 4 or more).

Data Analysis

Data was analyzed using SPSS Version 22. Comparisons between the FASD/PAE no mental health (FASD/PAE -MH) and FASD/PAE with mental health (FASD +MH) groups on each risk factor were initially calculated to determine the relationship between risk factors and mental health. Correlations between risk factors and outcome variables were calculated and frequency data analyzed. Logistic regression analyses were performed using the enter method to determine the relationship between risk factors (explanatory variables) and internalizing mental health disorders (ADHD, ODD/conduct disorder), externalizing mental health disorders (anxiety, depression, PTSD, attachment disorder), and total number of mental health disorders.

Results

Prevalence

Overall, 58.4% (n = 122/209) of children and adolescents with FASD/PAE had a mental health diagnosis, 36.4% (n = 76/209) had an externalizing co-morbidity, 10.5% (n = 22/209) had

an internalizing co-morbidity, and 11.5% had both (*n* = 24/209). The most common co-morbidities diagnosed in this sample were ADHD (46.9%, *n* = 98/209), followed by Anxiety (10.5%, *n* = 22/209), Attachment Disorder (9.6%, *n* = 20), ODD or Conduct Disorder (7.7%, *n* = 16/209), PTSD (7.7%, *n* = 16/209), and Depression (6.2%, *n* = 13/209). Of the 122 with a mental health diagnosis, 62.3% (*n* = 76) had an externalizing disorder, 18.0% (*n* = 22) had an internalizing disorder, and 19.7% (*n* = 24) had both. In addition, 34.4% (76/209) of children in this sample were at risk for a mental health diagnosis, including 14.4% (30/209) of children and adolescents with FASD/PAE without a mental health disorder diagnosed. Overall prevalence of mental health problems in this sample of children and adolescents with FASD/PAE represented 72.9% (*n* = 152/209) with a mental health diagnosis or emerging issue. See Table 1.2 for rates of mental health issues. I noted that sleep issues were significantly more common among children and adolescents with both FASD/PAE and a mental health co-morbidity (23.1% *n* = 38/122), relative to those without a mental health diagnosis (11.5%, *n* = 10/87) (see Table 1.1). Males *were not* significantly more likely than females to be diagnosed with a mental health co-morbidity, $x^2(1, 122) = 0.04$ ($p = .842$). Age at assessment correlated significantly with an internalizing disorder, $r(209) = .27$, $p<0.00$, suggesting that children and adolescents with FASD/PAE assessed at a later age were more likely to have a internalizing diagnosis.

Table 1.2

Overall prevalence of mental health problems in all children and adolescents with FASD/PAE

Mental Health (MH) Co-morbidities	Diagnosed (*n*)	At-risk (*n*)[a]
Total number of children	58.4% (122/209)	36.4% (76/209)
Externalizing disorder	62.3% (76/122)	34.2% (26/76)
Internalizing disorder	18.0% (22/122)	60.5% (46/76)
Both types of disorders	19.7% (24/122)	5.3% (4/76)
ADHD	**46.9% (98/209)**	**8.1% (17/209)**
Preschool 0-5 years	17.3% (17/98)	35.3% (6/17)
Child 5-12 years	68.4% (67/98)	58.8% (10/17)
Adolescent 13 to 17 years	14.3% (14/98)	5.9% (1/17)
% female (n)	42.9% (42/98)	41.2% (7/17)
ODD/CD	**7.7% (16/209)**	**6.2% (13/209)**
Preschool 0-5 years	0 (-)	53.8% (7/13)
Child 5-12 years	87.5% (14/16)	38.5% (5/13)
Adolescent 13 to 17 years	12.5% (2/16)	7.7% (1/13)
% female (n)	31.3% (5/16)	30.8% (4/13)
Depression	**6.2% (13/209)**	**3.3% (7/209)**
Preschool 0-5 years	0 (-)	0 (-)
Child 5-12 years	30.8% (4/13)	42.9% (3/7)
Adolescent 13 to 17 years	69.2% (9/13)	57.1% (4/7)
% female (n)	46.2% (6/13)	57.1% (4/7)
Anxiety	**10.5% (22/209)**	**10.5% (22/209)**
Preschool 0-5 years	0 (-)	0 (-)
Child 5-12 years	72.7% (16/22)	90.9% (20/22)
Adolescent 13 to 17 years	27.3% (6/22)	9.1% (2/22)
% female (n)	59.1% (13/22)	50.0% (11/22)
PTSD	**7.7% (16/209)**	**2.9% (6/209)**
Preschool 0-5 years	6.3% (1/16)	16.7% (1/6)
Child 5-12 years	75.0% (12/16)	33.3% (2/6)
Adolescent 13 to 17 years	18.7% (3/16)	50.0% (3/6)
% female (n)	37.5% (6/16)	66.7% (4/6)
RAD/Attachment disorder	**9.6% (20/209)**	**6.2% (13/209)**
Preschool 0-5 years	15.0% (3/20)	7.7% (1/12)
Child 5-12 years	85.0% (17/20)	53.8% (7/13)
Adolescent 13 to 17 years	0 (-)	38.5% (5/13)
% female (n)	40.0% (8/20)	46.2% (6/13)
Number of diagnoses		

1 diagnosis	51.6% (63/122)	-
2 diagnoses	28.7% (35/122)	-
3 diagnoses	13.9% (17/122)	-
4+ diagnoses	5.8% (7/122)	-

Table represents the number of children diagnosed or at-risk for a MH diagnosis.

[a] Number of children at risk for a mental health issues represents 46/76 (60.5%) children with a mental health diagnosis, and 30/76 (39.5%) children with no mental health diagnosis.

Participant characteristics

Prenatal and postnatal scores. Results are presented in figures 1.1-1.2. **C**hildren with FASD/PAE - MH were compared to children with FASD/PAE + MH on their prenatal and postnatal scores assigned at the time of their FASD assessment based on the FASD 4-digit code. Children with FASD/PAE + MH were significantly more likely to have a postnatal score of 4 (high risk), 53.8%, $p = .038$, and a prenatal score of 4 (high risk) approached significant, 49.0% $p = .058$, indicating that children with FASD and mental health issues are more likely to experienced prenatal and postnatal adversity.

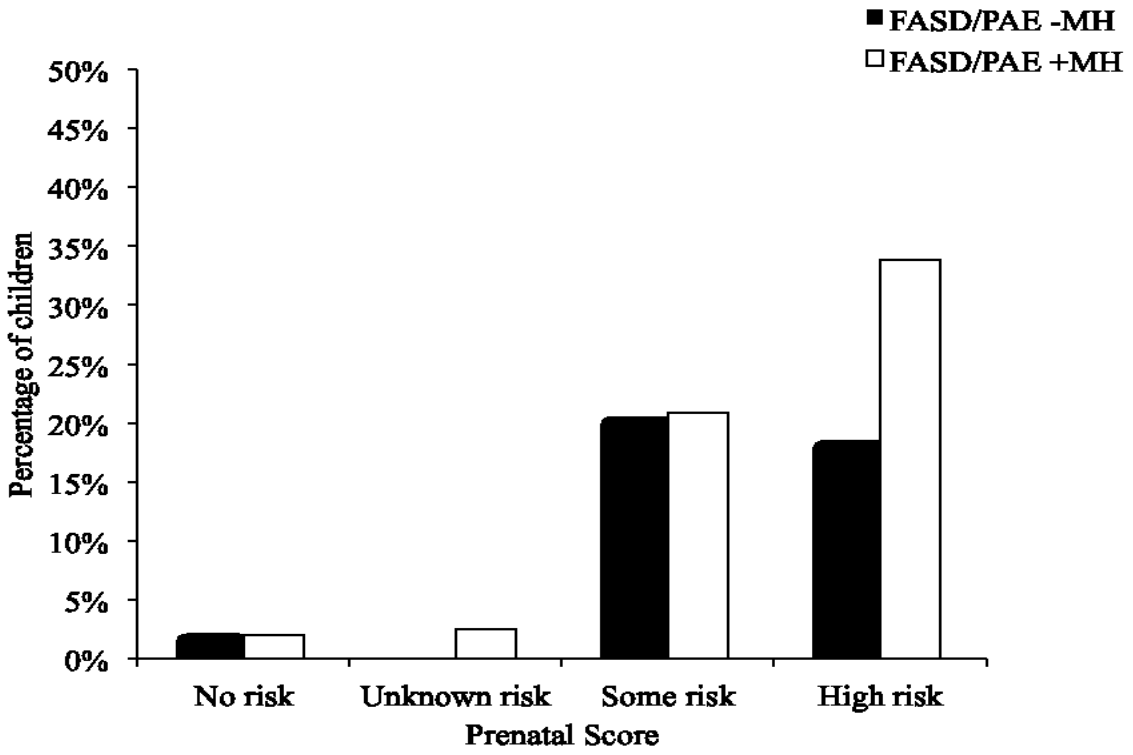

Figure 1.1 Percentage of children with a prenatal score between 0 (no risk) and 4 (high-risk)

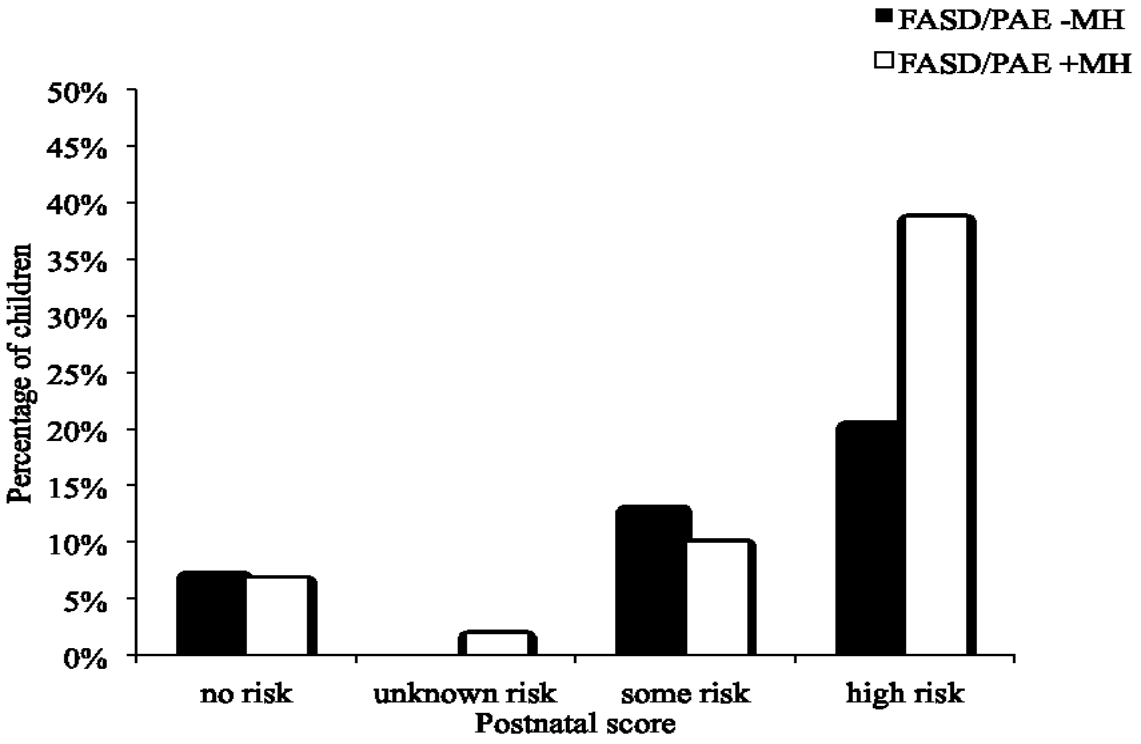

Figure 1.2 Percentage of children with a postnatal score between 0 (no risk) and 4 (high-risk)

Adverse Childhood Experiences (ACE)

Next, I compared children and adolescents with FASD/PAE – MH to those with FASD/PAE + MH on their Adverse Childhood Experience Scores (ACE). Findings revealed that children and adolescents with FASD/PAE +MH had significantly higher ACE scores, relative to those with FASD/PAE –MH (see Table 1.5). Of note, 54.7% of children with FASD/PAE +MH had an ACE score of 4 or greater, relative to 39.8% of those with FASD/PAE –MH. See Figure 1.3.

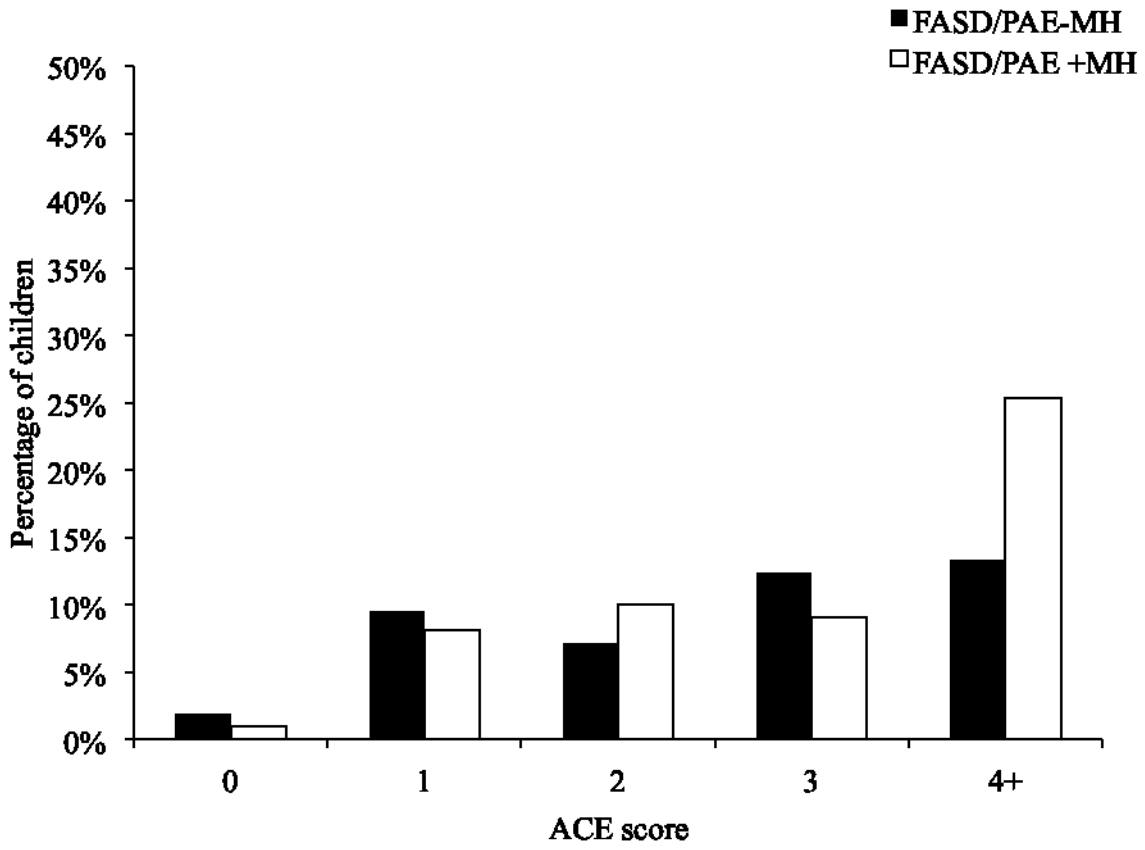

Figure 1.3 ACE scores for children with FASD/PAE-MH as compared to FASD/PAE+MH

Risk factors. Comparisons were made between children and adolescents with FASD with and without a mental health diagnosis based on family characteristics (see Table 1.3),

prenatal characteristics (see Table 1.4), and postnatal characteristics (see Table 1.5). Findings revealed that children and adolescents with FASD and a mental health co-morbidity were significantly more likely to have a parent with a history of behavioral issues or ADHD, substance/drug misuse problem, a history of maternal drug misuse during pregnancy, higher gestational birth weight, lived in more home placements, ever experienced physical or emotional abuse, and lived in a home with domestic violence.

Table 1.3

Main family characteristics of FASD/PAE and FASD/PAE + MH group

Family Characteristics	FASD – MH (*n*=87)	FASD + MH (*n*=122)	*p-value*
Bio mom education			.996
Ref: Elementary or junior high school	32.4% (35)	32.8% (43)	
Partial high school	24.1% (26)	25.2% (33)	
High School	7.4% (8)	7.6% (10)	
Post Secondary or University	7.4% (8)	6.1% (8)	
Unknown	28.7% (31)	28.5% (37)	
Bio parent FASD	17.2% (15)	27.9% (34)	.273
Both confirmed % (n)	24.1% (21)	24.6% (30)	
Bio parent learning difficulties	66.7% (58)	54.1% (66)	.068
Both confirmed % (n)	24.1% (21)	24.6% (30)	
Maternal mental health/emotional issues % (n)	46.0% (40)	40.2% (49)	.402
Bio parent behavior problem or ADHD % (n)	21.8% (19)	68.9% (42)	.048*
Both confirmed % (n)	4.6% (4)	10.7% (13)	
Bio parent trouble with the law % (n)	28.7% (25)	39.3% (48)	.113
Both confirmed % (n)	9.3% (10)	13.0% (17)	
Bio parent alcohol abuse problem	81.6% (71)	85.2% (104)	.211
Both confirmed % (n)	36.8% (32)	49.2% (60)	
Bio parent substance/drug use problem	67.8% (59)	79.5% (97)	.044*
Both confirmed % (n)	31.0% (27)	50.0% (61)	

[a] Data was analyzed using analysis of variance (ANOVA)
[b] Data was analyzed using chi square statistic

Table 1.4.

Main prenatal characteristics of FASD/PAE and FASD/PAE + MH groups

Prenatal Risk Factor	FASD – MH (*n*=87)	FASD + MH (*n*=122)	*p-value*
Maternal age at birth *Mean* (range)	24.16 (14-38)	23.67 (15-40)	.643
Missing % (n)	36.7% (32)	33.6% (41)	
Gestational length (weeks)			.214
Ref: Full Term	59.8% (52)	62.0% (85)	
Premature <37 weeks	20.7 (18)	12.3% (15)	
Missing % (n)	19.5% (17)	18.0% (22)	
Gestational weight in grams (n)	2928 (77)	3169 (103)	.018*
Missing % (n)	13.0% (10)	15.5% (19)	
Head circumference in cm (range)	33.69 (24-53)	34.02 (26-38)	.456
Missing % (n)	31.0% (27)	34.4% (42)	
Para mean (range)	2.0 (0-7)	2.4 (0-8)	.163
Missing % (n)	28.7% (25)	33.6% (25)	
Gravida mean (range)	3.7 (1-13)	4.2 (1-10)	.195
Missing % (n)	27.6% (24)	35.0% (42)	
Apgar Score 1 minute (range)	7.6 (4-9)	7.5 (1-10)	.789
Below normal <7 % (n)	18.2% (4)	24.9% (14)	
Missing % (n)	74.7% (65)	54.1% (66)	
Any complications during pregnancy	35.5% (31)	47.5% (56)	.119
Smoking during pregnancy (Ref: yes)	67.8% (59)	69.7% (85)	.609
Substance misuse during pregnancy	59.4% (49)	73.3% (90)	.011*
Unknown % (n)	0.5% (1)	-	

[a] Data was analyzed using analysis of variance (ANOVA)
[b] Data was analyzed using chi square statistic

Table 1.5 Main postnatal characteristics of FASD/PAE and FASD/PAE + MH groups

Postnatal Risk Factor	FASD – MH (*n*=87)	FASD + MH (*n*=122)	*p-value*
Living situation			.083[a]
% in biological home (n)	55.7% (49)	37.2% (45)	
% in foster care (n)	27.3% (24)	38.8% (47)	
% in adoptive care	15.9% (14)	19.8% (24)	
Mean number of placements (range)[a]	2.9 (1-10)	4.3 (0-24)	.002[b]*
Time in current placement in years (range)	5.5 years (4mos - 16 yrs)	5.1 years (2mos - 16 yrs)	.516[b]
Multiple moves	25.3% (22)	27.9% (34)	.678

Major changes in life circumstance	73.6% (64)	67.2% (82)	.324
Neglect	42.5% (37)	51.6% (63)	.194
History of physical/sexual/emotional abuse (yes or suspected)	41.6% (87)	58.4% (122)	.004[a]*
Household Dysfunction			
Not raised by both biological parents	40.2% (35)	20.0% (24)	.001*
Ever lived in fostercare	30.2% (26)	64.4% (47)	.186
Living Situation			
Substance abuse in home	63.2% (55)	68.9% (84)	.395
Bio parent trouble with the law	28.7% (25)	39.3% (48)	.113
Household member serious mental issue			
Current caregiver	22.6% (19)	16.5% (20)	.101
Biological parent	41.6% (43)	58.4% (54)	.768
Domestic Violence in home	20.6% (18)	40.1% (49)	.012*
Other household dysfunction not specified	21.8% (19)	32.0% (39)	.107
Mean ACE score (range)	3.2 (0-7)	3.9 (0-9)	.007*

[a] Data was analyzed using analysis of variance (ANOVA)
[b] Data was analyzed using chi square statistic

Correlations

I calculated correlations with risk factors and the main outcome variables internalizing co-morbidities and externalizing co-morbidities. Internalizing disorder significantly correlated with age at assessment, r(209) = .27, $p < 0.00$, intellectual ability of child above the borderline range, r(197) = .16, $p = .025$, but not with gender, ($p = .575$), FASD or PAE diagnosis ($p = .898$), child sleep issues ($p = .083$). Externalizing disorder significantly correlated with FASD or PAE diagnosis, r(209) = .14, $p = .048$, intellectual ability, r(197) = .14, $p = .047$, sleep issues, r(208) = .23, $p < 0.01$, but not with age at assessment ($p = .793$), child intellectual ability above the borderline range ($p = .092$), gender ($p = .575$). Results for correlations between internalizing or externalizing disorder and prenatal or postnatal factors are presented in tables 6.1a-6.1b.

Table 1.6a

Correlations between internalizing or externalizing co-morbidity and prenatal factors

Risk Factor	Internalizing *r* (p-value)	Externalizing *r* (p-value)
Prenatal score	0.08 (0.28)	0.03 (0.64)
Poor prenatal care (yes)	0.01 (0.94)	0.05 (0.49)
Maternal age (years)	-0.04 (0.67)	0.01 (0.87)
Gestational age (weeks)	-0.04 (0.69)	0.08 (0.41)
Type of delivery natural or other	0.01 (0.86)	-0.07 (0.35)
Head circumference in cm	0.01 (0.95)	0.06 (0.45)
Gestational weight in grams	0.01 (0.86)	0.16 (0.03)*
Para (number of pregnancies carried to term)	-0.11 (0.24)	0.17 (0.06)*
Gravida (number of pregnancies)	-0.06 (0.48)	0.18 (0.04)*
Smoke during pregnancy (yes)	-0.02 (0.80)	0.02 (0.74)
Drug exposure during pregnancy (yes)	0.08(0.25)	0.15 (.004)*

Note: dichotomous variables, no (0) yes (1)

* <. 05

Table 1.6b

Correlations between internalizing or externalizing co-morbidity and postnatal factors

Risk Factor	Internalizing *r* (p-value)	Externalizing *r* (p-value)
Postnatal score	0.23 (.010)*	0.01 (.860)
ACE score	0.29 (<.001)**	0.04 (.580)
Living in fostercare (yes/no)	0.14 (.040)*	0.06 (.380)
Single or both parents	0.15 (.040)*	0.18 (.010)*
History of physical/sexual/emotional abuse (yes or suspected/no)	0.30 (<.001)**	0.04 (.530)
Experienced neglect (yes or suspected/no)	0.21 (.030)*	-0.02 (.730)
Exposure to violence in home (yes or suspected/no)	0.25 (<.001)**	0.04 (.508)
Lived in a home with drugs and alcohol (yes or suspected/no)	0.18 (.090)*	-0.03 (.660)

Caregiver mental health issues (yes/no)	0.07 (.320)*	-0.10 (.140)
Bio mom mental health issue (yes or suspected/no)	0.01 (.890)	-0.01 (.870)
Bio parent behavioral problems (yes or suspected/no)	0.18 (.080)	0.10 (.140)
Bio parent ADHD	0.00 (.980)	0.14 (.040)*
Bio parent trouble with the law (yes or suspected/no)	0.14 (.010)**	0.04 (.550)

Note: dichotomous variables, no (0) yes (1)
*< .05
**< .01

Logistic Regression Results

Risk factors for internalizing or externalizing disorder diagnosed were examined using a logistic regression model. Odds ratios were calculated for prenatal and postnatal risk factors individually for internalizing and externalizing mental health outcomes, presented in tables 1.7a-1.7b. Age at assessment, sex (male/female), FASD diagnosis (yes/no), intellectual ability below borderline (yes/no), sleep issues (yes/no), and only prenatal or postnatal factors that significantly correlated with type of mental health diagnosis were included in the analysis (see tables 1.6a-1.6b). Findings revealed that postnatal environmental risk factors had the strongest influence on internalizing disorders, relative to prenatal risk factors. Compared to children and adolescents with FASD/PAE without an internalizing co-morbidity, age at diagnosis was associated with increased risk for being diagnosed with an internalizing diagnosis by 1.2 times. Experiencing any type of abuse emerged as the most influential single risk factor, increasing risk for having an internalizing disorder by 4 times. Experiencing neglect, living in a single parent home, and living in a home with violence or drug and alcohol abuse increased risk for an internalizing disorder by 2 to 3 times. Living in fostercare, having a bio parent with behavioral problems or trouble with the law emerged as protective factors, as compared to children with FASD and no internalizing mental health disorder. Accumulative ACE scores were also examined. Results revealed that an

accumulative ACE score 0-10 increased risk for an internalizing disorder by 1.4 times, relative to those children with FASD but no internalizing diagnosis. Children with FASD that had experienced 4 or more ACEs were 4.1 times more likely to receive and internalizing diagnosis, relative to those who experienced 3 or fewer ACEs.

In contrast, children with externalizing disorders had a higher incidence of prenatal risk factors, relative to those with FASD and no externalizing disorder. Sleep issues emerged as the most influential risk factors, increasing risk for an externalizing disorder by 3.1 times. Gestational weight, gravida, and drug exposure during pregnancy emerged as significant risk factors, increasing risk for an externalizing disorder by 1 to 1.8 times, relative to children with FASD without an externalizing disorder. Living with both parent's or caregiver's emerged as a protective factor, relative to children with FASD but no externalizing mental health diagnosis.

Table 1.7a

Unadjusted odds ratios of risk factor associated with having an internalizing disorder (0 = no, 1 = yes) among children with FASD/PAE.

Variables	Internalizing Co-morbidity OR[#] (95% CI)	*p-value*
Age at assessment	1.20 (1.09, 1.32)	<.001**
Sex (Being male)	1.22 (0.53, 2.35)	.556
Diagnosis (Being diagnosed with FASD)	1.12 (0.53, 2.38)	.530
Intellectual ability < borderline (yes)	0.43 (0.20, 0.91)	.027*
Ace score (0-10)	1.44 (1.20, 1.72)	<.001**
Aces (Having 4 or more ACEs endorsed)	4.12 (1.96, 8.68)	<.001**
Sleep issues	1.89 (0.92, 3.91)	.085
Living in fostercare (no)	0.50 (0.25, 0.97)	.041*
Single or both parents	2.48 (1.04, 5.93)	.042*
History of any type of abuse (yes or suspected)	4.36 (2.18, 8.72)	<.001**
Experienced neglect (yes or suspected)	2.82 (1.41, 5.62)	.003*

Exposure to violence in home (yes or suspected)	3.43 (1.74, 6.76)	<.001**
Lived in a home with drugs and alcohol (yes or suspected)	2.92 (1.27, 6.66)	.011*
Caregiver mental health issue (yes or suspected)	1.25 (0.49, 3.17)	.642
Bio parent behavioral problems (yes or suspected)	0.39 (0.20, 0.77)	.006*
Bio parent trouble with the law (yes or suspected)	0.44 (0.23, 0.86)	017*

Odds ratios (OR) less than 1 = protective, greater than 1 = risk. Risk factors for categorical variables correspond to 0 = no and 1 = yes, and continuous variables included age, gestational age, prenatal and postnatal score, ACE score.

*< .05
**< .001

Table 1.7b

Unadjusted odds ratios for each risk factor associated with externalizing disorder in FASD/PAE

Variables	Externalizing Co-morbidity OR[#] (95% CI)	*p-value*
Age at assessment	1.01 (0.94, 1.09)	.792
Sex (being male)	0.85 (0.49, 1.47)	.573
Diagnosis (being diagnosed with FASD)	0.97 (0.52, 1.81)	.959
Intellectual ability < borderline (yes)	0.61 (0.34, 1.08)	.092
Sleep issues (ref: no sleep issues)	3.13 (1.58, 6.23)	.001*
Ace score (4 > ACEs endorsed)	0.91 (0.53, 1.56)	.722
Single or both parents	0.44 (0.23, 0.82)	.010*
Bio parent ADHD (yes or suspected)	0.64 (0.31, 1.17)	.144
Gestational weight	1.0 (1.00, 1.01)	.030*
Para (number of pregnancies carried to term)	1.2 (0.99, 1.49)	.060
Gravida (number of pregnancies)	1.19 (1.01, 1.41)	.040*
Drug exposure during pregnancy	1.88 (1.04, 3.40)	.030*

*< .05

Adjusted odds ratios were calculated for selected prenatal and postnatal risk and protective factors and internalizing or externalizing co-morbidity (see tables 1.8a and 1.8b). Alpha level was set at .001 to adjust for multiple comparisons made on the main outcome variable. Predictor variables with a p-value >.001 and/or missing data above 10% were not entered into the model. Since the categories for ACEs are putatively intercorrelated (Dube et al., 2003; Chapman et al., 2007), I used the ACE score to assess the relationship of the accumulative impact of these adverse childhood experiences and mental health outcomes. I adjusted for age and sex in both models. Results for final models using logistic regression analyses are presented in Tables 1.8a-1.8b.

Table 1.8a.

Adjusted logistic regression analysis results for risk factors associated with internalizing disorders, controlling for sex.

Variables	Internalizing (*n* = 209) Odds Ratio (OR)[#] (95% CI)	*p-value*
Model 2 enter ACE score (overall = 79.4%)		
Age at assessment	1.24 (1.11, 1.73)**	.000
ACE score (0-10)	1.42 (1.16, 1.73)**	.001
Bio parent behavioral problems	2.36 (1.08, 5.12)*	.031
Sex (being male)	0.83 (0.39, 1.75)	.617

** p < .01
* p < .05

Table 1.8b.

Adjusted logistic regression analysis results for risk factors associated with externalizing disorders, controlling for age and sex.

Variable	Externalizing Co-morbidity OR[#] (95% CI)	*p-value*
Model (overall 59.6%); *n*= 209)		
Sleep issues	2.95 (1.46, 5.96)*	.003
Single or both caregivers (single parent home)	2.16 (1.13, 4.14)*	.021
Sex (being male)	0.86 (0.48, 1.53)	.619
Age at assessment	1.02 (0.93, 1.11)	.679

* $p < .05$

Discussion

In this study, I examined the association between various prenatal and postnatal risk factors and mental health outcomes diagnosed among children and adolescents with FASD/PAE. In this study, I explored whether prenatal and postnatal adversities are associated with externalizing and internalizing mental health disorders diagnosed in children and adolescents assessed for an FASD diagnosis. To address this, I looked at multiple risk factors and compared children and adolescents with FASD/PAE with and without mental health disorders diagnosed. I also used a large sample based on retrospective data since small sample sizes remains a common limitation.

Within the current sample, an astounding 58.4% of children and adolescents with FASD/PAE had received a mental health diagnosis and 36.4% of children were at risk for receiving a mental health diagnosis, including an additional 14.5% of children without a previously identified mental health co-morbidity. The most common co-morbidities represented in this sample included ADHD, anxiety, attachment disorder, ODD or conduct disorder, PTSD,

and depression. I also found that the total number of mental health co-morbidities ranged from 2 to 5 diagnoses, which highlights that the magnitude of mental health problems beginning at an early age in this population. The overall prevalence of mental health problems in this sample of children and adolescents with FASD/PAE represented 72.9% with a mental health diagnosis or an emerging mental health issue. These findings support previous studies suggesting that children and adolescents with FASD/PAE are at high risk for complex mental health problems. Given the young age of the sample these rates are likely an underestimate of the eventual mental health rates that may likely emerge with age.

Older age at assessment was significantly associated with internalizing diagnosis but not with externalizing diagnosis; younger children in this sample were rarely diagnosed with an internalizing disorder. This may reflect a barrier to obtaining a diagnosis for an internalizing disorder at a younger age as children with behavioral issues are more likely to be recognized and referred for a clinical assessment at a younger age than children presenting with internalizing issues. However, it remains the question as to whether internalizing issues diagnosed in later childhood reflect an emerging developmental problem that increases with age or whether internalizing issues emerge are more evident once existing services and supports in place are removed.

I also compared the prenatal and postnatal scores between children and adolescents with FASD/PAE with and without a mental health diagnosis. My findings revealed that children and adolescents presenting with a higher postnatal score are at risk for developing a mental health disorder, and therefore require an extensive mental health evaluation and further follow-up. I further examined the ACE scores in this sample and found an that 57% of children with a mental health disorder had experienced 4 or more ACEs during early childhood, as compared to those

with FASD/PAE without a mental health diagnosis. These findings imply that children and adolescents with FASD/PAE living in adverse environments are at high risk for developing severe adverse mental health or health problems in adult life (Anda et al., 2006).

Postnatal environmental risk factors were perhaps the strongest predictor for internalizing mental health disorders in this sample. Evidently, children and adolescents with FASD/PAE that have experienced physical abuse, neglect, witnessed domestic violence, or lived in a home with drugs or alcohol, a single parent, or parental mental health issues are likely at increased risk for developing an internalizing mental health disorder. Moreover, I found that those children that had experienced 4 or more ACEs had a 4 fold increased risk for being diagnosed with an internalizing disorder, relative to those children who had experienced 3 or less ACEs. These results are consistent with previous findings that have shown that risk for negative physical and mental health outcomes is greater among individuals that have experienced 4 or more ACEs (Anda et al., 2006). Furthermore, work from animal studies has shown that the interaction between chronic stress and ethanol exposure causes anxiety and depressive symptoms in rat models (Hellesmans et al., 2010). Hellesman et al.'s (2011) Stress-Diathesis hypothesis suggests that individuals with FASD/PAE exposure to multiple stressors over a period may be at increased vulnerability for developing psychopathology owing to an alcohol-induced predisposition. Therefore, it is possible that children with FASD/PAE that are raised in families experiencing significant adversity may be at higher risk for developing an internalizing disorder due to a combination of biological and environmental factors.

Among the prenatal risk factors beyond prenatal alcohol exposure, I found that gestational weight, number of pregnancies, and substance exposure during pregnancy were associated with having an externalizing diagnosis in this sample. Maternal substance use during

pregnancy such as cigarette smoking, marijuana, and illicit drugs have been associated with externalizing mental health issues in previous studies (Allen et al., 1998; Robinson et al., 2008; Linnet et al., 2003). However, I found no significant association between other prenatal substance exposures such as smoking during pregnancy and having an externalizing diagnosis, after controlling for other factors in my analyses. These results are consistent with previous cohort studies that have reported a significant association between prenatal alcohol exposure and externalizing behaviors in childhood and adolescence even after controlling for other factors (Larkby, Goldschmidt, Hanusa, & Day, 2011; Disney, Iacono, McGue, & Legrand, 2008; D'Onofrio et al., 2007).

Sleep issues emerged as a significant risk factor for having an externalizing mental health diagnosis. The trend for increased risk remained significant even after controlling for other factors. I also found that the association between sleep issues and having an internalizing mental health diagnosis approached significance. Previous studies on sleep issues in children with FASD have reported that children with sleep problems have higher activity levels and sensation seeking behaviours (Wengel, Hanlon-Dearman, & Fjeldsted, 2011). These findings suggest that sleep issues may be prevalent among children and adolescents with secondary mental issues and therefore would be a critical area for targeted intervention and improving mental health.

The finding that some postnatal environmental factors emerged as protective against having a mental health co-morbidity, highlights the need for broader recognition of emerging mental health issues during childhood. Factors relating to the quality of the caregiving environment such as living in a fostercare placement, biological parent with a history of behavioral or legal issues, may reflect the level of support received from systems of care that likely provide a buffer against developing a mental health problem. Furthermore, children and

adolescents with lower intellectual abilities (> 70) were at less risk for being diagnosed with an internalizing disorder. These results are consistent with Streissguth et al.'s (2004) findings, which identified that both an IQ score above 70 and older age at FASD assessment increased the risk for adverse life outcomes, including psychiatric issues, among patients with FASD, and most probably because children with prenatal alcohol exposure with cognitive, behavioral, and growing in a poor quality home are more likely to be referred for an assessment and to receive increased supports and intervention earlier. Furthermore, I found that living in home with two caregivers reduced the likelihood of receiving a mental health diagnosis. This finding may reflect that certain life circumstances such as living in a good quality home and reduced exposure to adversities such as stress and family life disruption can help increase resiliency against emerging mental health problems among children with FASD/PAE.

This work is the first study to examine risk and protective factors for mental health co-morbidities diagnosed in children and adolescents with FASD/PAE. Previous work has reported on risk factors associated with internalizing and externalizing behaviors (e.g. Fagerlund et al., 2012) but has been limited by smaller sample sizes and by examining few risk and protective factors. I addressed limitations in previous work by including a larger sample of children and adolescents with FASD/PAE. I also differentiated between the samples mental health status based on their clinical mental health diagnosis and not behavior in an attempt to tease apart children who are presenting with behavioral issues that are related to their FASD diagnosis from those with an FASD/PAE that are presenting with co-morbid issue. Although, these findings are consistent with previous studies and add to the growing literature on risk factors for adverse outcomes among the FASD population, caution is necessary in interpretation. I conducted a

study based on retrospective data, based on a clinically referred sample, and therefore results from this study may not be generalizable to all individuals within the FASD population.

One limitation to this approach is that I was unable to look at different types of mental health diagnoses separately within the analyses conducted because the number of children diagnosed were too few and therefore limiting power. Further work using larger sample sizes should be conducted in order to determine how risk factors may differ based on types of internalizing or externalizing disorders. Furthermore, birth charts were not available for all participants this study and therefore information on prenatal risk factors was incomplete for some of the sample, thus limited opportunity to fully explore prenatal risk factors associated with externalizing disorders. Some prenatal risk factors need to be further explored. For example, birth outcomes such as Apgar scores and detailed maternal factors such as stress, trauma, and mental health could not be evaluated in the current study, as detailed information was not available on all patients. There were also a number of children with unknown information about birth weight, which may have had an impact upon the findings. Therefore, further research should examine whether prenatal risk factors are strongly related to externalizing behavioral problems.

Despite these limitations, the findings from this study have practical and important therapeutic implications for addressing the mental health needs of children and adolescents living with FASD or PAE with a formal diagnosis. This study contributes to a complete understanding of emerging mental health issues in the FASD population. Findings from this study identified critical risk and protective environmental factors, which have been implicated in the psychopathology of mental health disorders in the general population. The consequent impact of environmental factors and prenatal alcohol exposure may be underappreciated among children

with FASD/PAE with internalizing behavioral issues. Many of the ACEs were strongly associated with internalizing disorders, which tend to be diagnosed as children grow older and likely when the issues become more severe and difficult to manage. There are currently no formal guidelines on mental health diagnosis and treatment within FASD/PAE. Therefore, ACEs may be a useful measure clinically for identifying children and adolescents with FASD/PAE that require specialized mental health supports and continued referral. Early assessment, stable home environment, and targeting sleep issues reported in children and adolescents with FASD may have important therapeutic implications for reducing externalizing and internalizing mental health issues among this population. Furthermore, it would appear that screening for emerging mental health issues among young children with confirmed prenatal alcohol exposure or suspected FASD may be critical for offsetting emerging mental health problems. Interventions targeting adverse prenatal and postnatal environmental influences can be expected to improve mental health outcomes for children and adolescents with FASD. Further work should continue to align mental health practice with an FASD/PAE to help better inform diagnosis and care.

In conclusion, this study identified risk factors associated with internalizing and externalizing diagnoses found in children with FASD/PAE, and provides increased insight into risk factors associated with the high prevalence of mental health disorders among children and adolescents with FASD/PAE. Further work should prospectively examine the association between risk and protective factors and mental health issues in large longitudinal samples.

CHAPTER IV

Profile of Neurobehavioral Functioning in Children and Adolescents with FASD/PAE with and without Mental Health Co-morbidity: preliminary findings at follow-up.

The most devastating aspect of prenatal alcohol exposure (PAE) is the central nervous system injury, which can manifest in a range of adverse neurobehavioral outcomes affecting children and adolescents with Fetal Alcohol Spectrum Disorders (FASD). FASD is a non-diagnostic term used to describe a continuum of outcomes observed across a spectrum of effects, including neuropsychological and behavioral problems. Children and adolescents with FASD can exhibit a variety of neurobehavioral impairments including deficits in intellectual ability, attention, processing speed, language, visual spatial abilities, academic achievement, executive functioning, learning, and memory (Mattson et al., 2011; Kodituwakku et al., 2009). Hence, these children and adolescents experience problems in areas important for independent function and therefore may contribute to the adverse outcomes observed in this population (Pei et al., 2011). Children and adolescents with FASD are also reportedly at higher risk for poor mental health outcomes or psychiatric problems (Pei et al., 2011 etc.). Specifically, estimated prevalence of mental health co-morbidities is observed at exceptionally high rates (Pei et al., 2011), affecting 94.2% of children and adolescents with FASD involved with the child welfare system (Chasnoff, Wells, & King, 2015), and between 67.2% to 63% for Canadian children diagnosed with FASD or prenatal alcohol exposure but no FASD diagnosis (McLaughlin et al., 2015; Tamana et al. 2015).

Mental health co-morbidities may carry many clinical implications and pose numerous challenges to obtaining an accurate diagnosis. Researchers have found that the degree of behavioral and emotional issues does not necessarily differ between those children and

adolescents with and without the facial dysmorphology required to diagnoses Fetal Alcohol Syndrome (FAS) (Mattson & Riley 2003; Roebuck et al., 1999). However, many children and adolescents with FASD are also diagnosed with ADHD, with rates up to 66% and in some cases higher, which can make it challenging to recognize and intervene appropriately (Mattson et al., 2011). For many children and adolescents with prenatal alcohol exposure or suspected FASD the rates of mental health diagnoses and other co-morbidities often go undiagnosed or misdiagnosed (Chasnoff et al., 2015; Coles et al., 2011), which can pose challenges to obtaining appropriate treatment and services. In a recent study, Chasnoff et al. (2015) found a significant change in mental health diagnoses post receiving a comprehensive FASD diagnosis. Children and adolescents with both FASD and a co-morbid mental health diagnosis may be difficult to treat and may present with unique needs and challenges. Furthermore, these mental health issues appear to persist and potentially worsen with age (Steinhausen & Spohr, 1998) or lead to more severe mental health psychopathology in later life (Pei et al., 2011). Notably, children and adolescents with FASD are frequently diagnosed with one or more co-morbid mental health disorder (Chasnoff et al., 2015; Burd et al., 2003). Thus, tools that are effective for screening the most common internalizing and externalizing co-morbidities are needed.

Prior research has indicated that children and adolescents with FASD and PAE exhibit a range of psychiatric symptomology. Ware et al. (2012b) found that children with heavy PAE exhibit similar rates for internalizing mental health disorders such as MDD and GAD to children with heavy PAE/ADHD, however, externalizing mental health disorders (i.e. CD and ODD) were significantly higher in children with heavy PAE/ADHD than children with heavy PAE only (Ware et al., 2012b). Roebuck et al. (1999) administered the Personality Inventory for Children (PIC, first edition) to caregivers of 32 children and adolescents (aged 3 to 16 years) with FAS or

heavy PAE. Relative to the control group of typically developing children, the children and adolescents with FASD showed significantly increased symptomology consistent with psychiatric, social, and cognitive issues. Specifically, children and adolescents with FASD had significantly higher T-scores on the depression, somatic complaints, delinquency, and psychosis subscales, as well as the cognitive abilities subscale that appeared similar across age groups. Their findings imply that children and adolescents with FASD are at risk for significant impairments in psychosocial functioning that span across early childhood to adolescence.

Externalizing behavioral problems have been most frequently described in children and adolescents with FASD (e.g. Coles et al., 1997a; Coles et al., 1999; Mattson & Riley, 2000; Nash et a., 2006; Sood et al., 2001; Steinhausen et al., 2003; Stevens et al., 2013; Ware et al., 2013). Researchers have shown that caregivers of children and adolescents with FASD/PAE report greater externalizing behavior problems than controls, resulting in elevated scores on scales measuring attention problems, aggressive behaviors (Coles et al., 1997; Mattson & Riley, 2000; Nash et al., 2006; 2011) hyperactivity, lying cheating, lack of guilt, disobedience, acts young for age (Nash et al., 2006; 2011), as well as social problems (Mattson & Riley, 2000). Other studies have reported similar findings among those with FASD as compared to those with confirmed PAE but no FASD diagnosis (Rasmussen et al., 2013; Roebuck et al., 1999). Furthermore, Mattson and Riley (2000) noted that 90.1% of children with PAE exhibited internalized and externalized problems that fell within the clinically significant range. Although externalizing behaviors are reportedly disproportionately greater in children and adolescents with FASD, many internalizing behaviors are also elevated as compared to typically developing children. Researchers have also described clinically significant internalizing issues including being anxious, depressed, and withdrawn (Roebuck et al., 1999; Matson & Riley, 2000; Rasmussen et

al., 2013; Stevens et al., 2013). Although, the differences in internalizing issues are reportedly small relative to externalizing issues there is ample evidence from both animal studies (Hellesman et al., 2010) and human studies (e.g. Haley et al., 2006; O'Connor & Paley, 2006; O'Leary et al., 2010; Sayal et al., 2007; Sood et al., 2001) that support a link between PAE and internalizing issues. Furthermore, some of the most common co-morbidities reported among children and adolescents with FASD include depression, anxiety, and mood disorders (Pei et al., 2011), as well as attachment disorders (O'Connor et al., 2002), and therefore further investigations are needed before concluding one domain is more impaired relative to the other (Pei et al., 2011; Mattson et al., 2011).

Other researchers have described a behavioral phenotype for FASD (see Korean et al., 2014 for a review). The Neurobehavioral Screening Tool (NST) was developed and validated using items from the Child Behavior Checklist (CBCL) that describe some externalizing behavioral problems such as tendency to act young for their age, less disobedient at home and so forth. Recent researcher examining the clinical utility and specificity of the tool have found that the NST can discriminate between young children with FASD from typically developing controls, and those with other behavioral disorders such as ODD/CD or ADHD (Nash et al., 2006; 2011; La France et al., 2014; O'Connor et al., 2015). Therefore, it is possible to conclude that some problem behaviors may be more likely related to FASD than other co-morbid issues. However, it is important to note that the NST is primarily used for screening children suspected of having an FASD and does not eliminate the need to further assess for co-morbidity with other mental health disorders. Furthermore, examining the *within* FASD profile would allow researchers to better identify the neurobehavioral features associated with FASD or a co-morbid disorder.

Currently there is a lack of empirical research comparing the behavioral phenotype *within* FASD, by comparing children and adolescents with FASD with and without mental health co-morbidity. To date, five studies have reported on the consequential impact of having an ADHD co-morbidity on neurobehavioral functioning in children and adolescents with FASD/PAE. Ware et al., (2012) compared the psychopathology and behavioral profiles of children with FASD (aged 8 to 16 years) and ADHD co-morbidity. They found that children and adolescence with FASD and ADHD co-morbidity were at increased risk for co-morbid conduct disorder and displayed more severe behavioral problems, as measured on the CBCL, as compared to those children without ADHD. More recently, researchers have begun to examine whether having an ADHD co-morbidity influences the cognitive functioning in children and adolescents with FASD. Boseck et al. (2014) compared the intellectual and adaptive abilities in a sample of children and adolescence with FASD and ADHD co-morbidity (mean age 10 years) as compared to those with ADHD but no PAE. Their findings revealed that children with FASD + ADHD showed a similar pattern of impairment but with significantly weaker intellectual abilities and adaptive skills as compared to children with FASD but no ADHD. Similarly, Raldiris et al. (2014), compared the intellectual abilities and behavioral profiles of four groups of children and adolescents (aged 6 to 16 years) with FASD, ADHD, FASD + ADHD, and other neuropsychological disorders. Their findings revealed children and adolescents with FASD and an ADHD co-morbidity performed significantly worse than children with ADHD only on the verbal comprehension subtest and displayed greater problem behaviors. In contrast, Glass et al. (2012) compared children with heavy PAE with and without ADHD on measures of IQ and EF. They found no significant differences between children with heavy PAE with and without ADHD co-morbidity. Rasmussen et al. (2010) found that having an ADHD co-morbidity had

little impact upon the neurobehavioral profile in a sample of children and adolescents with FASD. Although these findings suggest that co-morbidity may have little impact upon the pattern of neurobehavioral functioning in children and adolescents with FASD, this work has been limited by primarily focusing on concurrent ADHD despite the high risk for a number of other types of externalizing and internalizing co-morbidities. Furthermore, previous studies have been limited to one or two tools to measure psychopathology and behavior and/or cognitive functioning and have rarely examined the relationship between behavioral and cognitive measures. Hence, a more comprehensive picture of neurobehavioral functioning is lacking. Further examination of psychopathology and behavioral functioning in children and adolescents with FASD may provide insight into how to best screen for emerging mental health issues and intervene.

The Goal(s) of the Current Study.

In this current study, I report on the overall profile of psychopathological and behavioral functioning and performance on neuropsychological tests in a recruited sample of children and adolescents diagnosed with FASD or with confirmed history of PAE. Identifying the pattern of behavioral and cognitive impairments for children and adolescents with and without a mental health co-morbidity on a range of standardized measures will contribute to our understanding of the neurobehavioral profile of children with FASD/PAE and help identify priorities for targeted intervention.

I first examined the overall profile of neurobehavioral functioning among a sample of children and adolescents with FASD/PAE. I expected to find that the overall profile of neurobehavioral functioning would be significantly worse than the normative mean across all tests.

Secondly, I further examined the *within FASD profile by* comparing three groups of children: FASD/PAE no mental health diagnosis, FASD/PAE with an externalizing co-morbidity, and FASD with an internalizing co-morbidity. I anticipated that a unique pattern of behavioral and mental health problems would emerge among children and adolescents with FASD/PAE and a co-morbid mental health, compared to the FASD group. In particular, children and adolescents with FASD/PAE and externalizing co-morbidity would display greater behavioral issues, whereas those with internalizing co-morbidity would display greater emotional issues.

Thirdly, I compared differences between the three groups in performance on a range of standardized neuropsychological tests. I anticipated that children and adolescents with FASD/PAE and a mental health diagnosis would perform worse across all neuropsychological measures. I also expected to find that children and adolescents with FASD/PAE and an externalizing disorders would display greater deficits on measures of executive functioning and attention, whereas those with internalizing co-morbidity would display show greater impairments in face processing, memory, and processing speed, as compared to children and adolescents with FASD/PAE but no mental health co-morbidity.

Fourthly, previous studies reported a correlation between poor emotional processing and behavioral problems (e.g. Greenbaum et al., 2009). Therefore, I explored the correlation between caregiver reported mental health symptoms and neuropsychological measures.

Method

General Methods

Participants included children and adolescents with FASD or prenatal alcohol exposure (PAE) (n = 24) ranging in age between 9 to 19 years. All children were tested individually by a trained assessor on a neuropsychological battery of tests lasting about 2 hours. Participating children and caregivers also completed questionnaire(s) about mental health and behavior. Informed consent and assent were obtained from all participants and their caregivers/legal guardians, and all procedures were approved by the Health Research Ethics Board at the University of Alberta.

Participants

Twenty-four participants with a diagnosis of FASD or confirmed history of prenatal alcohol exposure were included in this study (see Table 2.1 for demographic characteristics). One participant did not complete all testing and decided to not continue with the study. I categorized the participants into three groups: children and adolescents with FASD/PAE but no mental health diagnosis (FASD - MH, n = 7), those with FASD and an externalizing co-morbidity (FASD/PAE + EXT, n = 9), and those with FASD and an internalizing co-morbidity (FASD/PAE + INT, n = 8). Mental health co-morbidities were confirmed based on formal clinical diagnoses made by trained clinicians during their initial FASD assessment or in the community prior referral into the study. A multi-method approach of diagnosing mental health disorders, including clinical interview, informant reports, and self-reports, and clinical observation, is accepted clinical practice and ensures that diagnoses are not overrepresented.

Participants were recruited through the Glenrose Rehabilitation Hospital FASD Clinic and/or were previously seen by the clinical team for an FASD assessment. All children seen for

an assessment by the Glenrose Rehabilitation Hospital FASD Clinic must have confirmed prenatal alcohol exposure from a reliable source determined by a review of prenatal history, birth documents, health records, and parental interviews. FASD diagnoses are made based on the 4-digit diagnostic code (Astley, 2004) and Canadian guidelines (Chudley et al., 2005) and diagnostic information is ranked using a 4-point Likert scale to independently rank growth deficiency, facial dysmorphology, brain dysfunction, and alcohol use. Information on Prenatal (e.g. genetic conditions, other substance exposures) and Postnatal (e.g. multiple placements, abuse) factors is also ranked. Confirmation of PAE is obtained through review of prenatal history, birth documents, health records, and parental interview. To receive a diagnosis for FASD using the 4-digit diagnostic code (Astley, 2004), children also have to demonstrate deficits in three or more neurobehavioral domains that include neurological signs, sensory-motor, communication, attention, cognition, academic achievement, memory, executive function, and adaptive functioning. All children are seen and assessed for FASD by a multidisciplinary team that includes a pediatrician, psychologist/neuropsychologist, speech-language pathologist, occupational therapist, and social worker to conduct the diagnostic assessment. Twenty children and adolescents had a confirmed medical diagnosis of FASD according to the 4-digit code, and four children and adolescents had prenatal alcohol exposure (PAE) but did not meet criteria for a medical diagnosis of FASD at the time of their initial FASD assessment. Prenatal and postnatal scores for unavailable for three children. Children scored 3 (29%, $n = 7$) or 4 (58.3%, $n = 14$) for prenatal factors but no children scored 2 or 1. Most children scored 4 (41.7%, $n = 10$) for postnatal factors, but some scored 3 (16.7%, $n = 4$), 2 (8.3%, $n= 2$), and 1 (20.8%, $n = 5$).

Table 2.1.

Summary of demographic characteristics for all children

Demographic characteristic	FASD/PAE (n = 24)
Sex (% female)	71.4%
Mean age (range)	13 yrs 9 mos (9-19yrs)
Diagnosis % (n)	
Fetal alcohol syndrome (FAS)	0%
Partial fetal alcohol Syndrome (pFAS)	8.3% (2)
Static encephalopathy: alcohol exposed	53.2% (13)
Neurobehavioral disorder: alcohol exposed	20.8% (5)
Prenatal alcohol exposure (PAE) (without a diagnosis)	16.7% (4)
Current living arrangement	
Biological Family	41.7% (10)
Adopted	33.3% (8)
Foster care	25.0% (6)
Mean number of placements (range)	2.6 (1 to 7)
Handedness N (% left)	29.2% (7)

Co-morbidities were confirmed based on information obtained from clinical file review and caregiver report (see Table 2.2). Children and adolescents in the externalizing co-morbidity group had confirmed and current diagnosis of attention deficit hyperactivity disorder (ADHD) and/or oppositional defiant disorder (ODD). Those children and adolescents in the internalizing group had a primary diagnosis of anxiety disorder, depression, and/or attachment disorder or reactive attachment disorder. *Of the internalizing group, 7 children* (*87.5%*) *with FASD/PAE also had a diagnosis of ADHD*, which is not uncommon given that ADHD is highly co-morbid with FASD as evidenced previous work (Rasmussen et al., 2010).

Exclusion criteria included children and adolescents with FASD with a known genetic disorder (e.g. Down Syndrome), neurodevelopmental disorder (e.g. autism spectrum disorder), motor/sensory impairment (i.e. cerebral palsy, blindness), or subsequent childhood head injury.

Table 2.2

Rates of Attention Deficit Hyperactivity Disorder (ADHD), oppositional defiant disorder (ODD), or conduct disorder (CD), depression (DEP), anxiety (ANX), obsessive compulsive disorder (OCD), post traumatic stress disorder (PTSD), and attachment disorders (ATTACH) for children with FASD/PAE with externalizing co-morbidities (**FASD/PAE +EXT**) and FASD/PAE with internalizing co-morbidities (**FASD/PAE +INT**).

Mental Health Diagnoses % (*n*)	FASD/PAE +EXT *n* = 9	FASD/PAE +INT *n* = 8
ADHD	88.9% (8)	87.5% (7)
ODD	22.2% (2)	12.5% (1)
ANX	0%	62.5% (5)
DEP	0%	10.0% (1)
OCD	0%	37.5% (3)
PTSD	0%	12.5% (1)
ATTACH	0%	50.0% (4)

I also documented information about the severity of co-morbidity reported in this sample of children. The total number of mental health diagnoses ranged from 0 to 3 (see Table 3.3). In addition to the mental health diagnoses, other co-morbidities were reported in 45% of this sample that include language disorder (25%), learning disability (8.3%), and seizure disorder (4.2%). Information about ongoing use of medication, mental health services, and parental history of mental health was also documented (see Table 2.4 for details).

Table 2.3

Percentage of children with FASD/PAE with 0 to 3+ mental health diagnoses

Number of diagnoses	% (*n*)
0	29.2% (7)
1	41.7% (10)
2	8.3% (2)
3+	20.8% (5)

Score of 0 indicates no mental health diagnosis and a score of 3+ indicates three or more mental health diagnoses.

Table 2.4

Summary of treatment and services for FASD/PAE with and without mental health groups

Mental health intervention/treatment	FASD /PAE - No MH (*n* = 7)	FASD/PAE + MH (*n* =17)
Currently receiving services % Yes (*n*)	13.3% (2)	86.7% (13)
Psychotropic Medications % Yes (*n*)	20.0% (3)	80.0% (12)
Psychiatry Services % Yes (*n*)	15.4% (2)	84.6% 11)
Individual Therapy % Yes (*n*)	0% (0)	35.3% (6)
Group Therapy % Yes (*n*)	0% (0)	17.6% (3)
Other family services e.g. respite, community program etc. % Yes (*n*)	0% (0)	29.4% (9)

Materials and Procedures

The study used standardized measures that are well regarded and psychometrically sound to measure each domain assessed, which included neuropsychological functioning, executive behaviors, psychopathology, and behavior. Scaled or z-scores based on age were used for the

dependent measure of neuropsychological functioning, and T-scores were for the dependent measure for behavioral functioning.

Children and adolescents completed a battery of neuropsychological tests to measure executive functioning, memory and working memory, attention, and face processing. All children completed the neuropsychological test battery with the exception of one child who was unable to complete the full testing session. Most subtests were age appropriate with the exception of the CVLT and therefore scaled scores were not available for all children. Caregivers completed a basic demographic questionnaire to gather information about the child's age, gender, ethnicity, and current mental health and treatment history. Caregiver reports on their child's behavioral and psychopathological functioning, and executive behaviors were completed.

Child Measures.

All children and adolescents with FASD/PAE completed a battery of neuropsychological tests and self-report questionnaire, as follows.

Neuropsychological Tests. ***Delis-Kaplan Executive Function System (D-KEFS).*** The D-KEFS (Delis, Kaplan, & Kramer, 2001) is a standardized neuropsychological battery suitable for individuals aged 8 years and through adulthood and assesses EF across nine domains. EF domains include flexibility of thinking, inhibition, problem solving, planning, impulse control, concept formation, abstract thinking, and creativity. D-KEFS yields scores that are reported in both raw scores and standard scores (account for age). D-KEFS has good reliability and validity and the subtests are able to detect executive function deficits in many clinical populations (Delis, Kramer, Kaplan, & Holdnack, 2004). Reliability studies of D-KEFS suggest that most subtests have adequate to high internal consistency and mostly adequate test retest reliability. The raw scores on each test are converted to age appropriate standard scores with a normative mean of 10

and standard deviation of 3. Participants completed the D-KEFS subtests as follows to assess three types of EF: card sort (Concept Formation), trail making test (Cognitive Flexibility), verbal fluency (Verbal EF), and color-word interference (Inhibition) tasks.

California Verbal Learning Test for Children (CVLT-C). The CVLT-C (Delis, Kramer, Kaplan, & Ober, 1994) is a standardized verbal learning and memory test appropriate for children aged 5-16 years. The test takes 15 to 20 minutes to complete and yields both raw and standard scores. Reliability studies of CVLT-C have demonstrated adequate to high internal consistency and test-retest reliability. The CVLT has been shown to have good validity in pediatric populations (e.g. Griffiths et a., 2006; Mottram & Donders, 2005). The raw scores on each test are converted to age appropriate standard scores with a normative mean of 100 and standard deviation of 15. Participants completed the CVLT-C to assess verbal learning and short/long delay free recall, and recognition abilities.

Automated Working Memory Assessment (AWMA). The AWMA (Alloway, 2007) is a computerized working memory battery suitable for ages 4 through 79 years, deigned to assess verbal and visuo-spatial and verbal and visuo-spatial working memory (WM) (depends on central executive and relevant short-term storage). Studies have shown adequate reliability ranging from .90-.79. There are total of 12 subtests. The AWMA has good construct and diagnostic validity in children (Alloway, Gathercole, Kirkwood, & Elliot, 2008). Participants completed the verbal WM (Digit Recall, Backward Digit Recall) and visuo-spatial WM (Block Recall) subtests, which lasted approximately 15 minutes.

Test of Variables of Attention (T.O.V.A.). The T.O.V.A. (Greenberg & Waldman, 1993) is a measure of sustained attention that is suitable for individuals aged six through adulthood. The computerized task takes between approximately 40 minutes to complete and yields both raw

and standard scores. Reliability and validity studies of the T.O.V.A. suggest high test-retest reliability and adequate validity in children with Attention Deficit Hyperactivity Disorder (Forbes, 1998). The raw scores on each test are converted to age appropriate standard scores with a normative mean of 100 and standard deviation of 15. Participants completed the visual attention subtest of the T.O.V.A., which lasted approximately 20 minutes.

Florida Affect Battery (FAB) The FAB (Bowers, Blonder, & Heilman, 1999) is a standardized neuropsychological test designed to measure two aspects of 'social cognition:' facial expressions and tone of voice. The neuropsychological test is suitable for use with both children and adults and covers three domains that include facial affect, prosodic, and cross modal. There are no available child (age 9-17 years) norms for this test. Although preliminary data has been collected on children aged 9-15 years (Slater, 2007). The test had been originally designed to detect disturbances in perception and understanding of emotional expression in neurologic or psychiatric populations. Reliability studies of FAB with adult cohort show high test-retest reliability. Participants completed the subtests measuring the facial affect domain as follow: facial affect naming, facial affect discrimination, facial affect discrimination tasks.

Caregiver Measures.

Caregivers completed a basic demographic questionnaire (see Appendix D) and parent reports about their child's psychopathology and behavior, and executive behaviors, which lasted approximately one hour.

Behavioral Reports. ***Behavioral Assessment System for Children Second Edition (BASC-2)***. The BASC-2 (Reynolds & Kamphaus, 2003) is a broad behavioral/emotional questionnaire that measures behavioral, emotional, and mental health of children aged 2 to 21 years. Scales of the BASC-2 include hyperactivity, aggression, conduct problems, atypicality,

anxiety, depression, somatization, withdrawal, attention problems, adaptability, social skills, and leadership. The BASC-2 has high internal consistency and test-retest reliability as well as good validity. This scale yields both raw and standardized scores (accounting for age). T-Score above 70 are considered elevated within the clinically significant range.

Personality Inventory for Children - Second Edition (PIC-2). All caregivers completed the PIC-2 (Wirt, Lachar, Klinedinst, Seat, & Broen, 2001), a comprehensive multidimensional measure of behavioral and emotional adjustment, family interaction, and academic functioning of children aged 5 to 19 years. The PIC-2 is referred to as a psychosocial measure that may be useful in predicting psychopathology. Scales of the PIC-2 include cognitive impairment, somatic concern, impulsivity/distractibility, psychological discomfort, delinquency, social withdrawal, family dysfunction, social skill deficits, and reality distortion. The PIC-2 has high internal consistency and test-retest reliability as well as good validity. This scale yields both raw and standardized scores (accounting for age). T-Score above 60-70 are considered elevated within the clinically significant range.

Behavior Rating Inventory for Executive Functioning (BRIEF). The BRIEF (Gioia et al., 2001) is an executive functioning rating scale completed by caregivers, appropriate for ages 5 to 18 years. The BRIEF measures three of areas of executive functioning based on parent report including Behavioral Regulation Index (BRI; inhibition, set-shifting, and emotional control), and Metacognition Index (MI; initiate, working memory, plan/organize, organization of materials, and monitor). The BRI and the MI combine to form the Global Executive Composite (GEC). The BRIEF also includes two validity scales to assess whether the informant has answered the questions in a consistent manner (Inconsistency Scale) or in an overly negative or pessimistic manner (Negativity Scale). The BRIEF is currently the only parent rating scale to assess

executive functioning, and has high validity (ranging from 0.80-0.98) and reliability scores (average 0.81). Both raw scores and scaled scores are yielded and scaled scores above 65 are considered elevated within the clinically significant range.

Statistical Analysis

Statistical analyses were conducted using the SPSS statistical package version 22 (SPSS, 2013). Standard scores were used for all main analyses (where available). Main subscale scores on the independent variables for the behavioral and neuropsychological measures were included for all analyses. Behavioral scores were analyzed using one-sample t-test(s) to compare scores of children and adolescents with FASD/PAE to the normative mean of 50. Differences in neuropsychological performance were analyzed using one-sample t-test to compare scores of children and adolescents with FASD/PAE to the normative mean of 10. Pearson's correlations between behavioral scores and scores on neuropsychological measures were conducted to examine the relation between the two. Descriptive analyses were conducted to report the percentage of children and adolescents that fell within the clinical range of on each of the behavioral measures. Smaller sample size limited some analyses conducted for the overall sample and subgroup analyses. The alpha level was set at .002 (i.e. 0.5/22) to adjust for multiple comparisons made on the main independent variables for the neuropsychological and psychopathology/behavioral scales. Furthermore, subgroup differences were not statistically compared on the demographic data and main independent variables since this required more statically power. Rather, descriptive analyses were conducted across the subgroups to examine trends on the main behavioral and neuropsychological scores and report the percentages of children and adolescents whose performance fell below one or more standard deviations below the mean.

Results

Correlations with age and sex were calculated for the main scaled scores for each behavioral and neuropsychological measure. Age correlated with performance on the D-KEF Verbal Fluency/Category Switching subtest ($r(22) = .59$, $p<0.01$) and the T.O.V.A. Reaction Time (RT) ($r(22) = .46$, $p<0.02$) subscales. These results indicate that younger children in the sample performed worse (relative to the norm) than older children on both measures. No other correlations between neuropsychological measures and potential covariates were found and therefore sex and age, were not considered in further analyses.

Results on Behavioral Measures

PIC-2. Participants displayed profound psychopathological issues on the main clinical scales of the PIC-2 (see Figure 2.1). Mean T-scores were significantly higher ($p = <0.00$) than the normative mean of 50 (using 99% confidence intervals) for each subscale except family dysfunction ($t(23)= 2.172$, $p = 0.04$). The majority of children had mean T-Scores in the clinically significant range of 60 and above the clinical range of 70 on each subscale except for family dysfunction (see Table 2.6). Table 2.7 shows the percentage of children whose scores on the PIC-2 main clinical subscales fell one or two standard deviations above the normative mean. Results indicate that the highest number of participants (>70%) showed psychopathological and cognitive problems on the cognitive impairment, impulsivity and distractibility, reality distortion, psychological discomfort, and social skills deficit subscales.

Table 2.5

Personality Inventory for Children Second Edition (PIC-2) results for all children with FASD/PAE (*n*=24).

Problem Scales	Mean	*SD*
Inadequate Abilities (COG 1)	**71.96**	10.28
Poor Achievement (COG 2)	**70.00**	8.39
Developmental Delays (COG 3)	**69.42**	17.41
Disruptive Behaviour (ADH 1)	**65.79**	12.01
Fearlessness (ADH 2)	53.29	10.95
Antisocial Behaviour (DLQ 1)	55.79	9.16
Dyscontrol (DLQ 2)	59.17	16.32
Noncompliance (DLQ 3)	**61.75**	11.45
Conflict Among Family Members (FAM 1)	55.71	11.71
Parent Maladjustment (FAM 2)	51.29	11.51
Developmental Deviation (RLT 1)	**78.08**	14.55
Hallucinations and Thought Deviations (RLT 2)	**71.25**	16.69
Psychosomatic Preoccupation (SOM 1)	**62.00**	15.18
Muscular Tension and Anxiety (SOM 2)	59.37	18.76
Fear and Worry (DSI 1)	**64.12**	11.78
Depression (DIS 2)	**68.20**	11.93
Sleep Disturbance/Preoccupation with Death (DIS 3)	**67.50**	14.89
Social Introversion (WDL 1)	**60.62**	13.26
Isolation (WDL 2)	**63.25**	17.03
Limited Peer Status (SSK 1)	**62.83**	9.85
Conflict with Peers (SSK 2)	**68.92**	17.52

i. Bold-face indicates above normative mean of 60 or 70, which indicates experiencing substantial difficulties range, as described by the PIC-2 tool.

ii. Underlined indicates experiencing problem behaviors in the clinical disturbance range, as described by the PIC-2 tool.

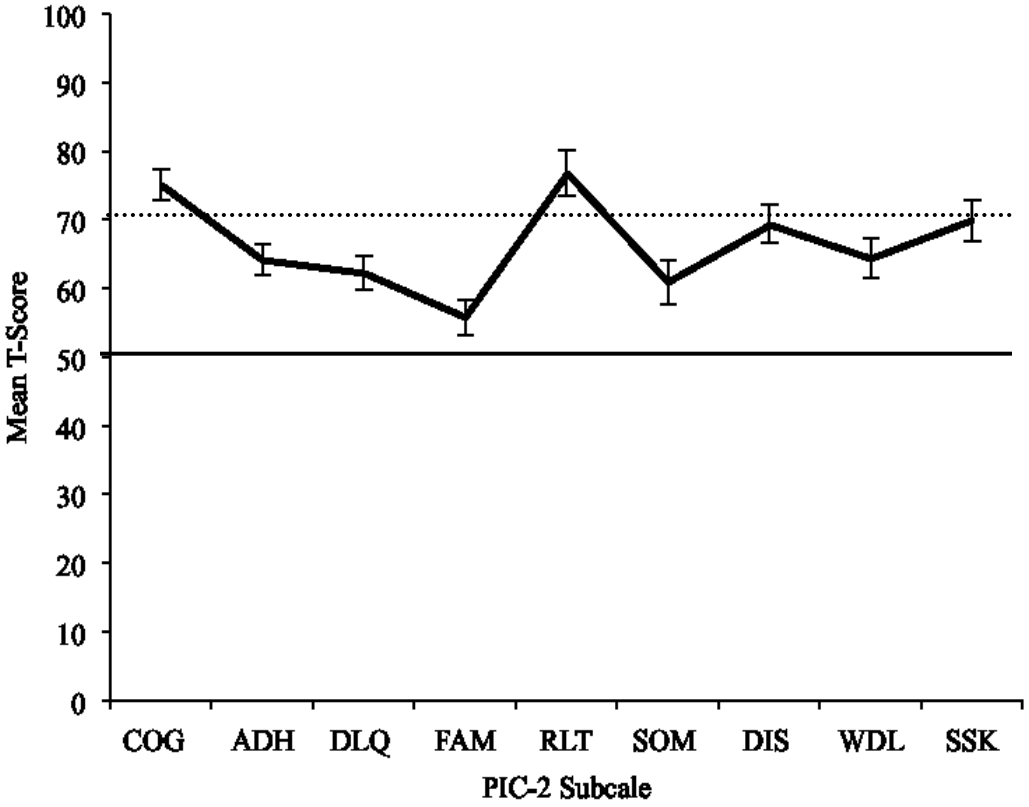

Figure 2.1 PIC-2 overall main subscales and standard error

BASC-2. Children with FASD/PAE displayed significant behavioral issues on the main composite scales on the BASC-2 (see Figure 2.2). Mean T-scores on the externalizing, internalizing, and behavioral symptom index scores were significantly higher ($p = <0.00$) than the normative mean of 50 (using 99% confidence intervals). Mean T-scores on the adaptive skills composite fell below the normative mean of 50 and the clinical mean of 40 ($p = <0.00$), indicating profound deficits in adaptive abilities (see Figure 2.2). Children with FASD/PAE displayed mean T-Scores above the clinically significant range of 60 on all subscales except aggression, conduct problems, somatization, and social skills (see Table 2.6). Table 2.7 shows the percentage of children whose scores on the BASC-2 composite scores fell one or two

standard deviations above the normative mean. Results indicate that the highest number of participants (>70%) showed behavioral problems on the behavioral symptom index and adaptive skills composites.

Table 2.6.

Descriptive data on the Behavioral Rating System for Children Second Edition (BASC-2) results for all children and adolescents with FASD/PAE (*n*=24).

Problem Scales	Mean	*SD*
Hyperactivity	**63.58**	14.28
Aggression	55.46	12.01
Conduct Problems	59.67	12.74
Anxiety	**61.50**	14.25
Depression	**62.08**	16.43
Somatization	56.37	12.27
Atypicality	**68.17**	19.00
Withdrawal	**63.79**	15.30
Attention	**60.79**	7.52
Adaptability	**38.50**	8.25
Social Skills	45.33	10.82
Activities of Daily Living	**38.54**	9.92
Functional Communication	**34.00**	8.16

i. Analyzed based on descriptive analyses

ii. Bold-face indicates above normative mean of 60 or 70, with the exception of adaptive scales where scores below 40 fall below the normative mean.

Cut-off scores reflect experiencing substantial difficulties and clinical disturbance respectfully.

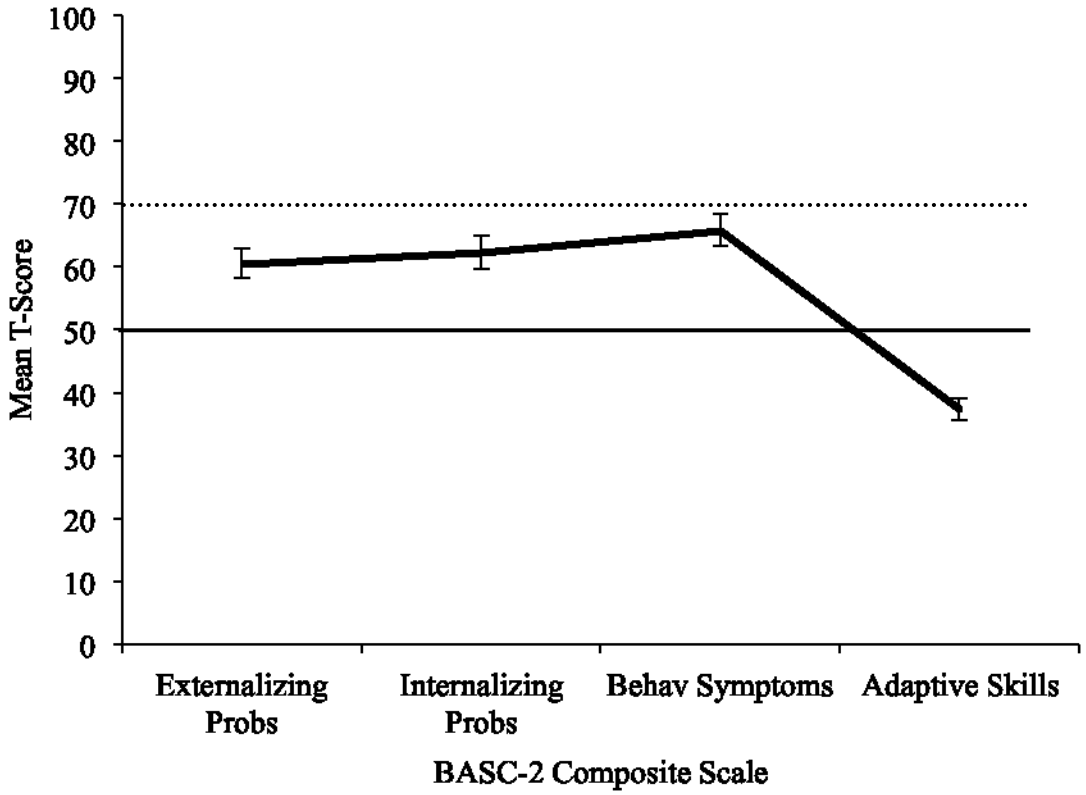

Figure 2.2 BASC-2 overall main subscales and standard error

Table 2.7

Percentages of children and adolescents with T-Scores above the at-risk (>T60) and clinically significant (>T70) range on the PIC-2 and BASC-2 parent rating scales.

Composite	*Above the Normative Mean*
Scales	
PIC-2 Cognitive impairment (*COG*)	75.2%
PIC-2 Impulsivity and distractibility (*ADH*)	71.0%
PIC-2 Delinquency (*DLQ*)	50.1%
PIC-2 Family dysfunction (*FAM*)	29.4%
PIC-2 Reality distortion (*RLT*)	83.5%
PIC-2 Somatic concerns (*SOM*)	46.1%
PIC-2 Psychological discomfort (*DIS*)	70.3%

PIC-2 Social withdrawal (*WD*L)	58.3%
PIC-2 Social skills deficits (*SSK*)	70.9%
Composite Scales	
BASC-2 Externalizing problems	58.7%
BASC-2 Internalizing problems	58.6%
BASC-2 Behavioral symptom index (*BSI*)	79.4%
BASC-2 Adaptive skills	70.8%

The BRIEF. Children with FASD/PAE displayed profound deficits on the main composite scores for the Global Executive Composite (GEC; t(21)= 10.165, p = <0.00), Behavioral Regulation Index (BRI: t(21)= 7.145, p = <0.00), and the Metacognitive Index (MI: t(21)= 9.164, p = <0.00). The GEC (*M* = 70.55, *SD* = 9.48), the BRI (*M* = 68.91, *SD* = 12.41), and MI (*M* = 69.55, *SD* = 10.00), index scales had means above the clinically significant range (>65).

Table 2.8

Descriptive data on the Behavior Rating Inventory for Executive Function (BRIEF) results for all children and adolescents with FASD/PAE (*n*=24).

Problem Scales	Mean T-score	*SD*
Inhibit	67.73	14.26
Shift	70.09	10.85
Emotional control	62.55	13.58
Initiate	66.09	9.13
Working memory	70.23	12.08
Plan/organize	70.50	8.60
Organization of materials	56.05	11.32
Monitor	67.68	9.81

Within FASD Profile

Trends on the PIC-2 and BASC-2 To examine differences among children with FASD/PAE, I examined data comparing three subgroups FASD/PAE-MH, FASD/PAE + EXT,

and FASD/PAE + INT to explore whether having a mental health diagnosis impacts neurobehavioral functioning. First, the three groups were compared on the substantive subscales and composite scores on the behavioral measures. T-scores analyzed on the PIC-2 included the substantive scales cognitive impairment (Cognitive Status), impulsivity/distractibility and delinquency (Externalizing Symptoms), family dysfunction (Family Dysfunction), reality distortion, somatic concerns and psychological discomfort, (Internalizing Symptoms), social withdrawal and social skills (Social Adjustment). T-scores analyzed on the BASC-2 included the composite scales externalizing problems, internalizing problems, behavioral symptom index (BSI), and adaptive skills. Multivariate Analysis of Variance (MANOVA) analysis for the overall group was not significant for the main dependent variables on the PIC-2 $F16,28) = .839$, $p = .636$, and on the BASC-2 $f(8,36) = 2.712$, $p = .019$. Follow-up exploration of the mean scores and percentages indicate that the children adolescents with FASD/PAE + INT group displayed greater problem behaviors on the PIC-2 Reality Distortion subscale, whereas the FASD/PAE + EXT group displayed greater problem behaviors on the externalizing problem scale (on the BASC-2).

Trends towards greater elevations were observed on five PIC-2 substantive subscales (see Figure 2.3). Children and adolescents with FASD/PAE + EXT and those with FASD/PAE + INT showed trends towards higher problem behaviors on three substantive scales relative to those with FASD/PAE but no co-morbid mental health. Children and adolescents with FASD/PAE + INT displayed elevated scores on Social Withdrawal ($M = 70.38$, $SD = 12.64$) and approached significance on Psychological Discomfort ($M = 73.13$, $SD = 16.63$), relative to the FASD/PAE + EXT and FASD/PAE- subgroups. Trends towards greater problem behaviors were observed on the four BASC-2 composite scores (see Figure 2.4) but did not reach significance. Children and

adolescents with FASD/PAE + EXT showed trends towards higher problem behaviors on the Adaptive Skills scale (*M* = 35.11, *SD* = 5.46), compared to the FASD/PAE + INT group, and those with FASD/PAE but no mental health diagnosis. Whereas, children with FASD/PAE + INT displayed higher behavioral problems on Internalizing problem scales (*M* = 66.25, *SD* = 13.16), relative to those with FASD/PAE +EXT and those with FASD/PAE but no mental health diagnosis.

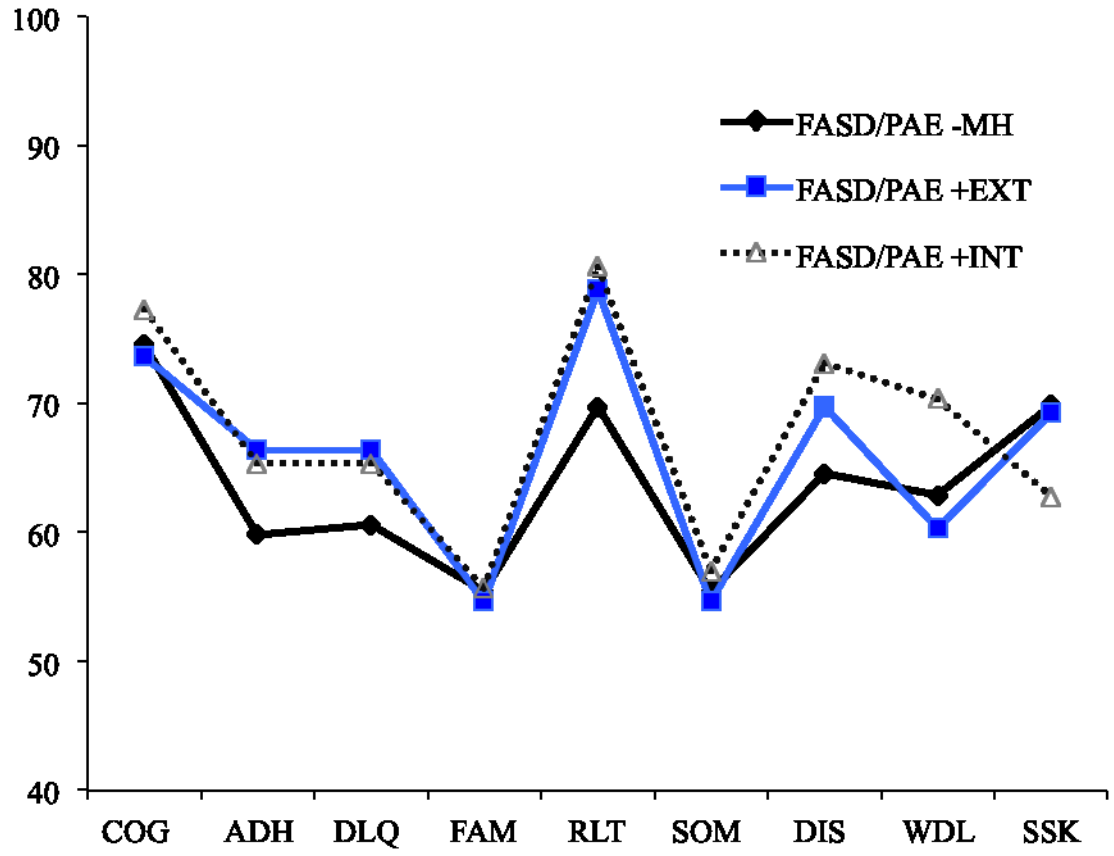

Figure 2.3 PIC 2 different subgroups and standard error

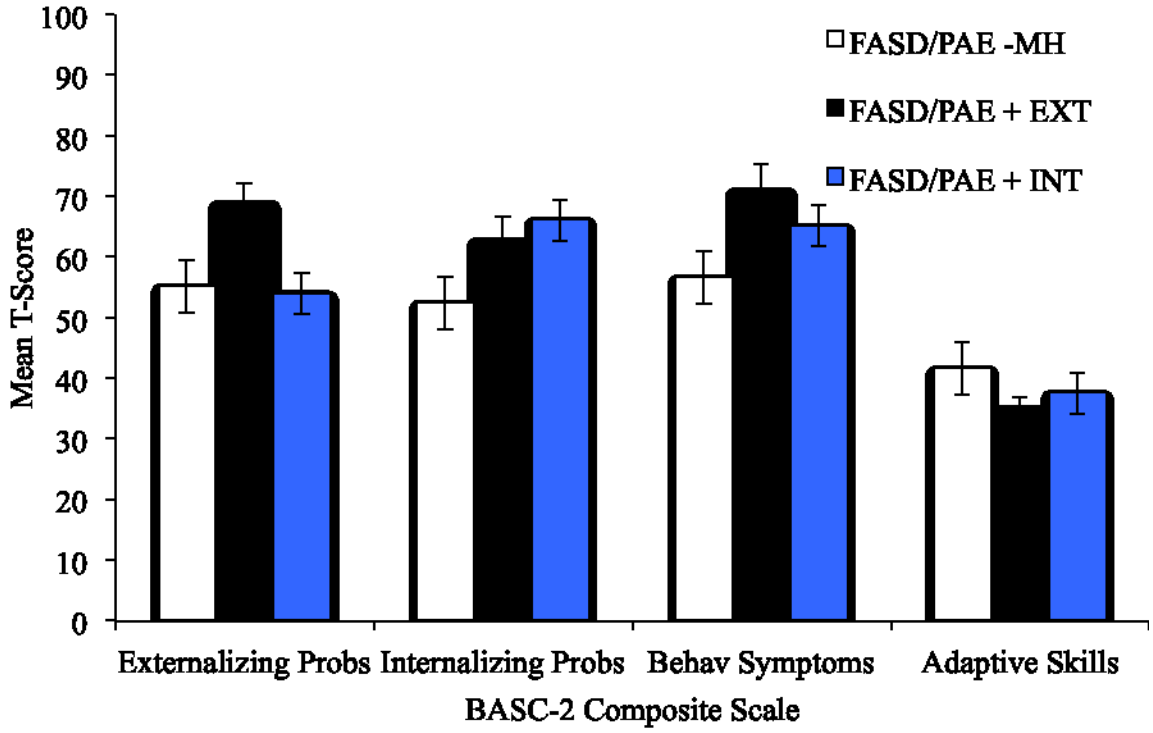

Figure 2.4 BASC-2 different subgroups and standard error

Results on Neuropsychological Measures

Standard scores analyzed included the D-KEFS number letter switching condition, category-switching condition, inhibition condition, inhibition-switching condition, card sorting correct sorts condition, card sorting description condition, card sorting recognition condition; CVLT-C learning trials 1-5 total correct; AWMA digit forward, digit backward, block recall; and the T.O.V.A. response time, and response time variability. Children with FASD/PAE performed significantly below the normative mean on measures of executive functioning, memory and learning, and working memory but significant differences were not observed on for the overall score on the sustained attention task ($t(22)= .186$, $p = .854$). However, further analyses on the error scores for the sustained attention task revealed that mean response time variability fell significantly below the normative mean of 100 (see Table 2.9). Next, raw scores were examined on the Florida Affect Battery subtests, which included facial affect recognition, facial affect

naming, and facial affect discrimination. Given that normative data for children up to age 17 years was not available, total number of errors were used and compared across the three tests. Children with FASD/PAE made the most errors on the affect discrimination task (M = 6), followed by the affect recognition (M =4), and affect naming (M = 2) tasks.

Table 2.9

Performance of children and adolescents with FASD/PAE (*n* = 24) on the D-KEFS subtests, CVLT-C, AWMA, and T.O.V.A. as compared to the normative mean.

Domain and observed variable/measure	FASD/PAE (*n* = 24) M (*sd*)	*t*	*Df*	*p*-value
Executive Functioning, *scaled scores* Mean = 10				
D-KEFS Trails Num/Letter Switching	5.46 (3.85)*	-5.787	23	<.001
D-KEFS Category Switching	8.29 (3.69)*	-2.269	23	.033
D-KEFS C/W Inhibition	7.43 (2.74)*	-4.483	23	<.001
D-KEFS C/W Inhib/Switch	6.87 (3.53)*	-4.249	23	<.001
D-KEFS Card Sorting Free Sort	7.61 (2.23)*	-5.141	23	<.001
D-KEFS Card Sorting Description	6.17 (2.33)*	-7.880	23	<.001
D-KEFS Card Sorting Recognition	5.17 (2.93)*	-7.890	23	<.001
Short and Long-term Memory				
CVLT-C Total T-Score Mean = 50	41.05 (11.14)*	-3.594	20	.002
Working Memory, *Scaled Scores* Mean =100				
AWMA Digit Forward	87.11 (11.90)*	-5.193	22	<.001
AWMA Digit Backward	87.35 (11.00)*	-5.416	21	<.001
AWMA Block Recall	84.35 (14.20)*	-5.286	22	<.001
Attention, *Scaled Scores* Mean = 100				
T.O.V.A. Response Time	100.78 (20.21)	.186	22	.845
T.O.V.A. Response Time Variability	75.30 (27.37)*	-4.325	22	<.001

i. Analyzed based on one sample t-test
* indicates <0.05

Within FASD/PAE Profile

Trends on the neuropsychological measures. I compared the neuropsychological profiles of three groups of children with FASD/PAE using scaled scores; FASD/PAE with no mental health diagnosis (FASD/PAE -), FASD/PAE with an externalizing disorder diagnosed representing ADHD and/or ODD (FASD/PAE + EXT), and FASD/PAE with an internalizing disorder diagnosed representing anxiety, depression, and/or attachment disorders (FASD/PAE + INT).

Mean performance on the neuropsychological measures revealed some interesting trends. Children with FASD/PAE +EXT performed worse on the D-KEFS Category Switching (*M* = 7.33, SD = 3.43), Color/Word Inhibition and Switching subtests (*M* = 5.56, SD = 3.17), relative to the FASD/PAE +INT and the FASD/PAE- subgroups. Whereas, the children and adolescents with FASD/PAE +INT showed lower scores on the D-KEF Trail-making Number-Letter Sequencing subtest (*M* = 4.25, *SD* = 2.77) relative to the other subgroups. Lower scores were observed on the CVLT-C Total score for the FASD/PAE +EXT (*M* = 38.77, SD = 12.38) and FASD/PAE +INT subgroups (*M* = 40.83, SD = 13.12), relative to the FASD/PAE- subgroup. Relative to both groups, mean performance for children and adolescents with FASD/PAE +EXT was lower for the T.O.V.A. Response Time Variability (M = 59.63, SD = 24.59) and lower for the T.O.V.A. Response Time (*M* = 87.13, *SD* = 20.99) although this score still fell within normal limits. In comparison to the FASD/PAE- group, children and adolescents with FASD/PAE +EXT (*M* = 67.25, *SD* = 24.68) and FASD/PAE +INT (*M* = 58.37, *SD* = 25.45) made more omission errors on the T.O.V.A. task, although performance for the FASD/PAE +INT was the weakest. Relative to both groups, children and adolescents with FASD/PAE +INT (M=74.12, SD) made more commission errors on the T.O.V.A. task.

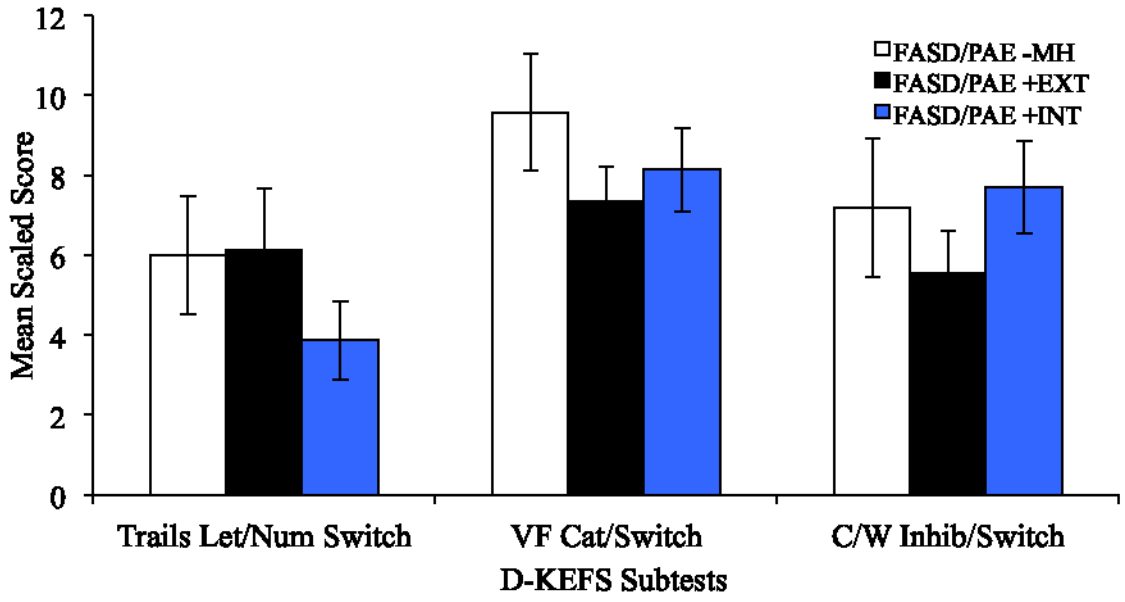

Figure 2.5 **Mean** performance of children and adolescents and standard error on the executive functioning measures for each FASD/PAE -, FASD/PAE + EXT, FASD/PAE + INT subgroups.

Main parent rating composite scores on the BRIEF were compared between the FASD/PAE -MH, FASD/PAE +EXT, and FASD/PAE + INT subgroups. Results revealed that children and adolescents with FASD/PAE +EXT tended to have higher scores on the BRI composite scale (*M*= 74.33, *SD* = 11.94), as compared to the FASD/PAE +INT (*M*= 64.57, *SD*= 12.09) and FASD/PAE- (*M*= 62.80, *SD*= 12.37) subgroups. However, children with FASD/PAE with and without a mental health diagnosis tended to show similar scores on the mental MI and GEC composite scales (see Table 2.10).

Next, I examined the mean scaled scores and percentages across the three subgroups FASD/PAE- MH, FASD/PAE +EXT, and FASD/PAE +INT are presented in Table 2.10. Performance of children 1 SD or more below the normative mean includes a standard score of 7 or below (D-KEFS), of 85 or below (AWMA), of 80 or below (T.O.V.A.; clinical range), or a T-

Score of 60 or less. Mean scores, standard deviations, and percentages of children below the normative mean or in the clinically significant range are reported in Table 2.10 for three groups of children.

Table 2.10

Percentage of children and adolescents whose performance was in the clinical significant range on the D-KEFS, CVLT-C, AWMA, T.O.V.A., and BRIEF measures for each FASD/PAE -MH, FASD/PAE + EXT, FASD/PAE + INT subgroups

Domain and measure	No Mental Health FASD/PAE-MH (*n* = 7)	Co-morbid Mental Health FASD/PAE + E (*n* = 9)	FASD/PAE + I (*n* = 8)
	% (M)	% (M)	% (M)
Executive Functioning, *Scaled Scores* M = 50			
D-KEFS Trails Num/Letter Switching	71.5 % (6.00)	44.4% (6.11)	87.5% (3.86)
D-KEFS Category Switching	28.6% (9.57)	55.5% (7.33)	25.0% (8.14)
D-KEFS C/W Inhibition	66.8% (7.17)	44.4% (7.33)	62.5% (7.43)
D-KEFS C/W Inhib/Switch	66.7% (7.17)	77.7% (5.56)	37.5% (7.71)
D-KEFS Card Sorting Free Sort	50.0% (7.00)	66.6% (6.78)	12.5% (9.00)
D-KEFS Card Sorting Description	83.4% (5.00)	100.0% (5.33)	37.5% (8.00)
D-KEFS Card Sorting Recognition	100% (4.33)	88.8% (4.44)	50.0% (6.63)
Short and Long-term Memory			
CVLT-C Total T-score	80.0% (45.40)	77.7% (38.77)	66.8% (40.83)
Working Memory, *Scaled Scores*			
AWMA Digit Forward	42.9% (84.50)	50.0% (86.78)	50.0% (85.01)
AWMA Digit Backward	71.5% (81.83)	37.5% (87.81)	42.0% (88.77)
AWMA Block Recall	28.6% (88.45)	50.0% (81.85)	50.0% (82.67)
Attention, *Scaled scores*			
T.O.VA. Response Time Variability	42.9% (85.67)	87.5% (66.16)	37.5% (80.25)
T.O.V.A. Response Time	0% (107.50)	50.0% (90.16)	0% (107.75)
T.O.V.A. Commission Error	28.6% (84.83)	50.0% (84.50)	62.5% (74.12)
T.O.V.A. Omission Error	62.5% (78.50)	42.9% (68.83)	62.5% (58.37)
Parent Report of Executive Functioning T-scores			
BRIEF BRI	40.0% (62.80)	77.7% (74.33)	42.90 (64.57)
BRIEF MI	60.0% (68.80)	66.6% (68.78)	71.5% (71.29)

BRIEF GEC	60.0% (67.00)	66.6% (72.00)	71.5% (70.00)

Note: Delis-Kaplan Executive Function System (D-KEFS), California Verbal Learning Test for Children, (CVLT), Automated Working Memory Battery (AWMA), Test of Variables of Attention (T.O.V.A.), Behavior Rating Inventory of Executive Functioning (BRIEF).

Correlations between Child and Parent Measures

Finally, I examined correlations between neuropsychological and behavioral measures. Correlations between neuropsychological and behavioral measures were calculated for the BASC-2 and PIC-2 and the D-KEFS, CVLT-C, T.O.V.A., AWMA, and BRIEF scaled scores. I found that the PIC-2 distractibility subscale significantly correlated with D-KEFS motor speed task ($r(23) = .464$, $p = .026$), cognitive impairment subscales correlated with and color word naming ($r(24) = .-.450$, $p = 0.27$) and color word reading ($r(24) = -.524$, $p = .009$) , and the BASC-2 internalizing subscale correlated with D-KEFS card sort correct sorts ($r(23) = .430$, $p = .040$). Negative correlations suggest that children performed poorer on these tasks had greater problem behaviors. The correlations between other neuropsychological tasks and the PIC-2 and BASC-2 subscales were not significant.

Next, I examined correlations between parent reported executive behaviors on the BRIEF and PIC-2 and BASC-2 subscales. See Table 2.11 for results.

Table 2.11

Correlation between T-scores on the Behavior Rating Inventory Executive Functioning (BRIEF) and the Behavioral Assessment System for Children (BASC-2) and Personality Inventory for Children (PIC-2) composite scale

Analyzed using Pearson's bivariate correlations

Composite scale	BRIEF BRI *r* (p-value)	BRIEF MI *r* (p-value)	BRIEF GEC *r* (p-value)
PIC-2			
Cognitive impairment (*COG*)	.31 (.151)	.55 (.008)**	.53 (.011)*
Impulsivity and distractibility (*ADH*)	.47 (.028)*	.43 (.045)*	.55 (.008)**
Delinquency (*DLQ*)	.62 (.002)**	.16 (.481)	.44 (.041)*
Family dysfunction (*FAM*)	.15 (.510)	.32 (.152)	.30 (.173)
Reality distortion (*RLT*)	.60 (.003)**	.38 (.082)	.58 (.004)**
Somatic concerns (*SOM*)	-.07 (.743)	.51 (.016)*	.32 (.142)
Psychological discomfort (*DIS*)	.69 (<.001)**	.23 (.304)	.54 (.009)**
Social withdrawal (*WD*L)	-.04 (.87)	.19 (.397)	.123 (.58)
Social skills deficits (*SSK*)	.50 (.019)*	.01 (.978)	.27 (.217)
BASC-2			
Externalizing problems	.72 (<.001)**	.34 (.122)	.62 (.002)**
Internalizing problems	.64 (.001)**	.348 (.113)	.58 (.005)**
Behavioral symptom index (*BSI*)	.81 (<.001)**	.51 (.016)*	.787 (<.001)**
Adaptive skills	-.46 (.028)*	-.44 (.039)*	-.55 (.008)**

* indicates <.05
** indicates p <.001

Discussion

The current study examined the neuropsychological and behavioral functioning in three groups of children and adolescents with FASD/PAE: 1) children with no mental health diagnosis, 2) children with an externalizing mental health diagnosis, and 3) children with an internalizing mental health diagnosis. I aimed to examine the impact of having a mental health diagnosis on four neurobehavioral domains including executive functioning, memory, attention, and behavior. As hypothesized, my findings indicate that children and adolescents with FASD/PAE and a mental health co-morbidity may display greater impairments characterized by poor executive

functioning skills involving switching, verbal fluency, and inhibition, learning and memory, attention and behavioral difficulties, but with relative strengths in working memory. These findings add to the growing literature describing the within FASD behavioral phenotype and associated domains that may be of greater importance in developing targeted strategies.

Behavioral domains

Overall, among all children and adolescents with FASD/PAE, there was a significant difference across the behavioral scales measured on the BASC-2 and PIC-2. For all subscales, the mean T-Scores differed significantly from the normative mean of 50. Clinically significant scores were observed on the BASC-2 externalizing, internalizing, behavioral symptom index, and adaptive abilities subscales, which confirm that these children display severe behavioral issues that reflect both the externalizing and internalizing domains. I also noted that mean T-scores on the PIC-2 subscales fell above the clinical normative mean of 60 on all main composites scales with the exception of family dysfunction. Most children in this sample were living in a stable home placement and therefore this result may not represent all families. Most common clinical problems observed in this sample include hyperactivity, anxiety, depression, inattention, atypicality, withdrawal, adaptive problems, reality distortion, and cognitive impairment.

I wanted to determine whether children and adolescents with FASD/PAE and a mental health co-morbidity display a distinct pattern of psychopathological difficulties on the PIC-2. Among the children and adolescents with FASD/PAE and internalizing co-morbidities a pattern of difficulties emerged on the PIC-2 with highly elevated scores displayed on the somatic concerns, psychological discomfort, and social withdrawal subscales, which is not surprising given that these areas collectively represent internalizing problem behaviors. In contrast, children

and adolescents with FASD/PAE and externalizing co-morbidities showed little impact of co-morbidity on behavioral functioning on most subscales as compared to the FASD/PAE no mental health group. Interestingly, I found that both internalizing and externalizing co-morbidity groups displayed highly elevated scores above T=70 on the reality distortion subscale, not observed in the FASD/PAE without a mental health diagnosis group. Roebuck et al. (1999) also noted that children with FASD/PAE were highly elevated on the reality distortion scale measured on the PIC first edition. My findings extend these previous results since it would appear that those children and adolescents presenting with a mental health co-morbidity are more likely to present with unusual thoughts or ideas and or developmental deviations, relative to those without a mental health diagnosis. Furthermore, I also noted a trend towards highly elevated scores on the psychological discomfort scale, which reflects negative affect associated with depression, mood, anxiety, and sleep issues, preoccupation with death. The psychological discomfort scale is a new subscale added to the PIC-2 subscale and therefore no previous known study investigating psychiatric profiles in children with FASD/PAE has reported elevations on this subscale. To my knowledge, no previous study has examined elevations in sleep disturbance, flat affect, and suicide ideation that may be associated with mental health co-morbidity in this population, and therefore emphasizes the need to examine the within FASD/PAE profile. Furthermore, elevations on the psychological discomfort subscale are consistent with elevations noted on the BASC-2 depression subscale in both the internalizing and externalizing subgroups. My results also revealed that children with FASD/PAE but no mental health co-morbidity displayed scores on the impulsivity and distractibility, family dysfunction, and somatic concerns subscales that fell within the normal range, and therefore these areas may be less problematic for children and adolescents with FASD/PAE without a mental health disorder.

I also examined the profile of mental health issues on the BASC-2 in children and adolescents with FASD/PAE with and without mental health co-morbidity. Comparisons among the three groups revealed that children and adolescents with FASD/PAE and an externalizing disorder displayed trends towards greater externalizing problems, relative to the other two groups. However, both the externalizing and internalizing mental health co-morbidity groups showed trends towards increased internalizing problems, behavioral symptoms, and poor adaptive skills, relative to those children without a mental health diagnosis. Although there were symptom overlap between the BASC-2 and PIC-2 measures in identifying a unique behavioral profile for those children and adolescents with FASD/PAE with and without mental health co-morbidity, it would appear that the PIC-2 detected additional symptoms that may be important for screening mental health co-morbidity in this population.

Neuropsychological domains

Overall, among all children and adolescents with FASD/PAE, there was a significant difference in performance relative to the normative mean across all measures. Children and adolescents with FASD/PAE were most impaired on executive functioning, memory, emotion processing, and sustained attention. These findings are consistent with previous studies that have found the most affected domains and involve more complex tasks that place higher demands on executive functioning (Bisanz & Rasmussen, 2009; Mattson et al 2010; Rasmussen et al., 2013; Tamana et al., 2014). In comparing the within FASD/PAE group profile, I found that children and adolescents with FASD and a mental health co-morbidity showed trends towards weaker performance on some measures of executive functioning. Children and adolescents with FASD/PAE and an internalizing disorder had greater difficulties on a task measuring cognitive flexibility and made more errors on a sustained attention task, whereas those with an

externalizing disorder had greater difficulty on tasks measuring inhibition and sustained attention. Both groups of children with FASD/PAE and a mental health disorder performed poorer on a task measuring verbal fluency, relative to children with FASD/PAE but not mental health diagnosis. However, I observed no significant differences on the working memory measures and a task measuring memory and learning, and therefore memory may not be key domain to assess when screening for strengths and challenges among children and adolescents with FASD/PAE with a mental health disorder. Previous studies have shown significant differences between children with FASD with and without ADHD on measures of IQ but not on neuropsychological tests measuring specific domains. One explanation may be differences in selection criteria when grouping children into subgroups. Previous studies have grouped children based on behavioral symptoms (e.g. Glass et al., 2013), whereas in the present study I used their clinical diagnosis. Furthermore, no previous work has looked specifically at children with FASD with an internalizing disorder and my findings suggest that these children may display a unique pattern of impairments on some tasks that have also been used in other studies.

Despite reporting elevated scores on the BRIEF questionnaire indicating executive behavioral problems, there was little impact of co-morbidity upon the executive behavior profile based on parent report. This suggests that informant ratings may not be sensitive to detecting the pattern of executive function and behavioral impairments that may emerge between subgroups of children and adolescents with FASD/PAE. For example, Gross et al. (2014) found no significant correspondence between parent reported executive behavior using the BRIEF questionnaire and objective measures. The lack of differences observed for executive behavior based on parent report highlights the need to use objective measures when assessing the executive functioning of abilities of children and adolescence with FASD/PAE.

Finally, I examined correlations between mental health measures and cognitive and executive behavioral measures. Executive behaviors measured on the BRIEF corresponded with several mental health symptoms most prominently representing the externalizing domain, but performance on the neuropsychological tasks correlated with few mental health symptoms. I observed interesting correlations between executive behaviors and externalizing behavioral problems. Results indicated that children and adolescents with parent-reported difficulties in behavioral regulation inhibition (i.e. set-shifting, emotional control) displayed greater externalizing behavior problems including delinquency, impulsivity, distractibility, hyperactivity, aggression, and conduct problems. As compared to other populations, my findings are consistent with previous studies that have reported correlations between parent reported behavior regulation difficulties and externalizing behavior problems (e.g. Jarratt, Riccio, & Siekierski, 2005). Furthermore, it appears that children and adolescents with parent reported difficulties in metacognitive skills (i.e. initiating, working memory, planning etc.) showed increased externalizing behavioral problems and poorer adaptive abilities. The fact that the correlations between these scales were moderate is consistent with the subtle differences in the performance on working memory measures between children and adolescents with FASD/PAE with and without mental health co-morbidity in this current study.

In contrast, few correlations were observed between internalizing behaviors and executive behaviors. Children and adolescents with FASD/PAE with parent reported difficulties in behavioral regulation exhibited increased internalizing problems such as depression, anxiety, fear, worry, mood and sleep disturbances, preoccupation with death, unusual thoughts. I also noted that those with parent reported difficulties with metacognitive skills displayed increased somatic complaints, fear, worry, depression, and sleep disturbances or preoccupation with death.

My findings suggest that based on parent ratings, caregivers possibly underreport behavioral problems among children and adolescents with FASD/PAE and internalizing co-morbidities. Although parent reported sources tend to highly correspond, the results are interesting and suggest that the use of mental health tools, parent behavioral reports, and neuropsychological measures may generate different needs of intervention depending on the concurrent mental health issue a child with FASD/PAE is presenting with.

Conclusions and implications

My findings add to the growing literature examining the *within* FASD profile on behavioral and neuropsychological measures. The preliminary results of this current study suggest that probable differences in neurobehavioral functioning between the three clinical groups within FASD/PAE exist, which implies that functioning may be exacerbated by co-occurring mental health issues and warrants further attention. Children with FASD/PAE and a mental health co-morbidity appear to be most profoundly impacted in their behavioral and executive functioning abilities, and subtler weakness in memory, emotion processing, and sustained attention. Notably, children and adolescents with FASD/PAE and a mental health co-morbidity performed worse on measures that placed more demands on executive functioning, as compared to those children with FASD/PAE and no mental health co-morbidity. This finding is consistent with previous reports of worse performance of children and adolescents on some more complex EF tests (Tamana et al., 2014; Rasmussen & Bisanz, 2009). Adolescence is a time of grave transition and often where adverse outcomes such as trouble with the law, school drop out, as well as mental health issues tend to emerge and potentially worsen. As these children age, their co-morbidities may worsen due to more changes in their EF abilities or the reverse. Subsequently, these areas may be targets for increased support and intervention to increase

resilience and prevent poor mental health outcomes. Future studies examining the relationship between brain-based factors and adverse outcomes such as mental health using larger sample sizes are needed. My findings highlight the need to conduct further research to determine whether there is a unique pattern of impairment between children with FASD/PAE with an externalizing co-morbidity versus those with an internalizing co-morbidity. Examining the profile of strengths and weaknesses between children with FASD/PAE with and without a mental health co-morbidity has important implications for clinical practice and particularly in identifying the presence of a mental health co-morbidity and intervening early as possible is important. An estimated 86.5% of children with prenatal alcohol exposure are often missed or misdiagnosed (Chasnoff et al., 2015). Further examining the within profile may help identify priorities for targeted intervention that could concurrently improve behavioral and cognitive functioning. Moreover, by comparing children and adolescents with FASD/PAE on clinical screening tool for assessing mental health issues it helpful for identifying tools helpful for unique screening approaches and in defining how mental health presents in youth with FASD/PAE. I acknowledge that there were limitations to this current study, which included small sample size, high number of children with FASD +ADHD in the internalizing co-morbidity group, and stratifying the sample into two co-morbidity groups. Future studies could address these limitations by including larger sample sizes and including potential covariates into the analyses. Further work should examine the relationship between scores on objective neuropsychological measures and parent and/or teacher behavioral and mental health ratings.

CHAPTER V

General Discussion

Early recognition of mental health issues emerging in childhood has long been recognized as crucial to preventing later adverse outcomes. Specifically, reducing the effects of significant adversity on children's mental health is critical to children's lifelong learning, health, and behavior. Although overwhelming evidence attests to the high rates of mental health issues associated with FASD/PAE, there is little evidence basis for remediating or preventing mental health issues in this population. This thesis research examined the association between mental health disorders diagnosed in children and adolescents with FASD/PAE with adverse environmental exposures, and impact on neurobehavioral functioning.

Findings from this Study 1 revealed that multiple risk factors are associated with internalizing and externalizing mental health disorders in children and adolescents with FASD/PAE. Postnatal risk factors such as experiencing physical abuse, neglect, witnessing violence, and parental history of legal or behavioral issues was strongly associated with developing an internalizing disorder. My findings also indicate that perhaps prenatal risk factors are more frequently associated with externalizing mental health diagnoses. I also identified that children at most risk for developing a mental health disorder were significantly more likely to have a high prenatal and postnatal score. Findings from Study 2 revealed that children and adolescents with FASD/PAE and a mental health co-morbidity show a unique pattern of behavioral and neuropsychological impairments. Behavioral data revealed that children and adolescents with FASD/PAE and a mental health disorder share overlap in some symptoms that may help screen children with FASD/PAE with a mental health disorder and develop more targeted interventions. I further examined the neurobehavioral profile to show that having an

internalizing co-morbidity appeared to exacerbate internalizing behavioral issues, whereas having an externalizing disorder had little impact on behavioral functioning. Neuropsychological data presented a profile of strengths and weaknesses that implicate executive functioning deficits as the main domain impacted by having a mental health diagnosis.

Findings from this study provides important evidence that could help increase opportunity for healthcare providers, educators, policy makers to screen for mental health issues for FASD/PAE and help ensure that children and adolescents living with FASD/PAE and their families are provided with optimal care and targeted intervention. The following section will summarize and discuss the relevance of these findings to improving clinical care, educational services, interventions, and policies that could help reduce adverse mental health outcomes and improve quality of life.

Practical Implications

Children and adolescents with FASD/PAE can often be missed, misdiagnosed, or untreated due to multiple factors including co-occurring behavioral and mental health issues. There are presently no formal guidelines on screening or diagnosis mental health among children and adolescents with FASD/PAE. However, findings from this study imply that due to the complexity that these children can present with it is important to examine mental health through an FASD/PAE lens by taking into account all information relating to their FASD/PAE diagnosis. Children and adolescents with FASD/PAE can still present with behavioral and emotional issues that are clinically significant and concur with their behavioral phenotype and not necessarily a secondary disorder. Developing a tool kit with mental health screening tools that community-based clinicians, physicians, and psychiatrists can be formally trained with would help with screening and identifying co-morbid issues early on. Results from this thesis work suggest that

perhaps using more than one tool and a more comprehensive psychiatric tool for older children with FASD/PAE would be more effective in detecting mental health issues in this population. Furthermore, providing a within FASD/PAE profile to help guide clinicians assessing children and adolescents with FASD/PAE would be helpful for improving evidence based practice. Currently, there is no formal role for a psychiatrist or clinical psychologist to work within an FASD/PAE Clinical Team to screen and diagnosis mental health issues as part of the FASD/PAE diagnostic process. More often, children and adolescents are referred on for a mental health assessment by a mental health team. Yet, the current literature suggests that as these children grow older there is an increased need to screen for mental health, which may require specialized training and knowledge within FASD/PAE.

Secondly, data from this study suggests that perhaps some of the behavioral issues relate to the underlying executive impairments. Two approaches to developing remediation for mental health issues are necessary for designing interventions to better address the unique needs for this population. Firstly, children and adolescents with FASD/PAE behavioral and mental health issues could be improved by implementing neurorehabilitative interventions targeting executive functions. Two promising interventions developed and adapted for children and adolescents with FASD are the Alert Program (Nash et al., 2012) and the Go Far program (Coles, Kable, Taddeo, & Strickland, 2015). Both programs target self-regulation leading to improvements in executive functioning (Nash et al., 2012), adaptive, and disruptive behavioral problems (Coles et al., 2015). Secondly, would be to adapt mental health therapies to increase treatment adherence and clinician capacity to administer therapy to an FASD/PAE population. One approach would be to provide therapeutic strategies for psychiatrists, psychologists, and social workers can implement and incorporate within their practice. Currently, there is no existing research adapting mental

health therapy targeting anxiety and depression in a format that can be administered by a clinician within their clinical practice. Mental health intervention development is imperative for building capacity for clinicians to provide services to the FASD/PAE population and ultimately improve outcomes.

There are also important implications for caregivers that may often feel perplexed and overwhelmed by their child's co-morbid diagnosis in addition to having an FASD. Caregivers may not easily recognize their child's behavior as a result of an interaction between environmental factors and the neurodevelopmental characteristics of their child. Therefore, translating findings from this work into accessible knowledge for caregivers could be helpful and may help empower caregivers in advocating for their child. There is also a need for children and adolescents with FASD and their caregivers to receive a family-centered approach to intervention and care to help strengthen protective factors and ultimately enhance a positive developmental trajectory.

Conclusion

Although the prevalence of mental health issues have long been recognized in the mental health population, children and adolescents with FASD/PAE continue to live with complex mental health issues years beyond receiving an FASD/PAE diagnosis. Evidence-based practice for dealing with mental health issues in children and adolescents with FASD/PAE has been lacking. Increasing capacity to screen and treat mental health issues in children and adolescents with FASD/PAE would help ensure that affected children are identified early on and receive the targeted range of service they may need to help offset later, more complex issues.

References

Achenbach, T. M. (1982). *Developmental psychopathology* (2d ed.). New York: Wiley.

Achenbach, T. M, & Edelbrock, C. S. (1978). The classification of child psychopathology: A review and analysis of empirical efforts. *Psychological Bulletin*, *85*, 1275-1301.

Alberta Children Services, (2006). *Fetal alcohol spectrum disorder*. Retrieved from http://child.alberta.ca/home/594.cfm.

Alberta Alcohol and Drug Abuse Commission (ADDAC) (2004). *Estimating the rate of FASD and FAS in Canada*. Retrieved from http://corp.aadac.com/content/corporate/for women/women_info_estimating_fasd.pdf.

Allen, N. B., Lewinsohn, P. M., & Seeley, J. R. (1998). Prenatal and perinatal influences on risk for psychopathology in childhood and adolescence. *Development and Psychopathology*, *10*, 513-529.

Alloway, T. P. (2007). *Automated working memory assessment*. Oxford: Harcourt.

Alloway, T. P., Gathercole, S. E., Kirkwood, H., & Elliott, J. (2008). Evaluating the validity of the Automated Working Memory Assessment. *Educational Psychology: An International Journal of Experimental Educational Psychology*, *28*(7), 725-734.

Alloway, T. P., Gathercole, S. E., Willis, C., & Adams, A. M. (2004). A structural analysis of working memory and related cognitive skills in young children. *Journal of Experimental Child Psychology, 87*(2), 85-106.

American Academy for Pediatrics of Substance Abuse and Committee on Children's Disabilities, (2000). Fetal alcohol syndrome and alcohol-related neurodevelopmental disorders. *Pediatrics*, *106* (2:1), 358-61.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental*

disorders. 5th edition, text revision. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders.* 4th edition, text revision. Washington, DC: American Psychiatric Association.

Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C., Perry, B. D., Dube, S. R., & Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. *European Archive of Psychiatry and Clinical Neuroscience*, *256*, 174-186.

Aragon, A. S., Kalberg, W. O., Buckley, D., Barela-Scott, L. M., Tabachnick, B. G., & May, P. A. (2008). Neuropsychological study of FASD in a sample of American Indian children: processing simple versus complex information. *Alcoholism: Clinical and Experimental Research*, *32*(12), 2136–2148.

Archer, T, Beninger, R. J., Palomo, T., & Kostrzewa, (2010). Epigenetic and Biomarkers in the Staging of Neuropsychiatric Disorders. *Neurotoxicity Research*, *17*, 347-366.

Archibald, S. L., Fennema-Notestine, C., Gamst, A., Riley, E. P., Mattson, S. N. & Jernigan, T. L. (2001). Brain dysmorphology in individuals with severe prenatal alcohol exposure. *Developmental Medicine & Child Neurology*, *43*, 148-54.

Astley, S. J. (2004). *Diagnostic guide for fetal alcohol spectrum disorders: The 4-digit code*. 3rd Eds. University of Washington, Seattle: FAS Diagnostic and Prevention Network.

Astley, S. J. (2010). Profile of the first 1,400 patients receiving diagnostic evaluations for fetal alcohol spectrum disorder at the Washington State fetal alcohol syndrome diagnostic & prevention network. *The Canadian Journal of Clinical Pharmacology, 17*(1), e132-64.

Astley, S. J., & Clarren, S. K. (2000). Diagnosing the full spectrum of fetal alcohol-exposed individuals: Introducing the 4-digit diagnostic code. *Alcohol and Alcoholism*, *35*(4), 400-

10.

Autti-Rämö, I., Autti, T., Korkman, M., Kettunen, S., Salonen, O., & Valanne, L. (2002). MRI findings in children with school problems who had been exposed prenatally to alcohol. *Developmental Medicine and Child Neurology*, *44*(2), 98–106.

Barron S., & Riley, E. P. (1992). The effects of prenatal alcohol exposure on behavioral and neuroanatomical components of olfaction. *Neurotoxicity Teratology*, *14*(4), 291-297.

Barker, D. J. P. (1992). The fetal origins of adult hypertension. *Journal of Hypertension*, *10*, S39-S44.

Barker, D. J. P. (1999). The fetal origins of type 2 diabetes mellitus. *Annals of Internal Medicine*, *130*, 322-324.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*(1), 65-94.

Barkley, R. A. (2002). Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder. *Journal of Clinical Psychiatry*, *63*(12), 10-15.

Benz, J., Rasmussen, C., & Andrew, G. (2009). Diagnosing fetal alcohol spectrum disorder: History, challenges and future directions. *Paediatrics & Child Health, 14*(4), 231-237.

Belsky, J, & Pluess, M. (2009). Beyond diathesis-stress: differential susceptibility to environmental influence. *Psychology Bulletin*, *135*, 885–908.

Belsky, J., Bakermans-Kranenburg, M. J., & Van Jzendoorn, M. H. (2007). For better and for worse. Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, *16*, 300–304.

Birmaher, B., Ryan, N. D., Douglas, E., Williamson, B. A., Brent, D. A., Kaufman, J., Dahl, R. E., Perel, J., & Nelson, B. (1996). Childhood and Adolescent Depression: A Review of

the Past 10 Years. *Journal of the American Academy of Child and Adolescent Psychiatry*, *35*(11), 1427-1439.

Boyd, T. A., Ernhart, C. B., Greene, T. H., Sokol, R. J., & Martier, S. (1991). Prenatal alcohol exposure and sustained attention in the preschool years. *Neurotoxicology and Teratology, 13*(1), 49-55.

Bourke, C., Douglas, K., & Porter, R. (2010). Processing of Facial Emotion Expression in Major Depression: A Review. *Australian and New Zealand Journal of Psychiatry*, *44*, 681-696.

Bos, K. J., Fox, N., Zeanah, C. H., & Nelson, C. (2009). Effects of early psychosocial deprivation on the development of memory and executive function. *Behavioral Neuroscience*, *16*(3), 1-7.

Bos, K., Zeanah, C. H., Fox, N. A., Drury, S. S., McLaughlin, K. A., & Nelson, C. A. (2011). Psychiatric Outcomes in Young Children with history of Institutionalization. *Harvard Review in Psychiatry*, *19*, 15-24.

Bowers, D. Blonder, L. X., & Heilman, K. M. (1999). *Florida Affect Battery*. Gainesville, FL: University of Florida.

Bronfenbrenner, U., & Ceci, S. (1994). Nature-Nurture Reconceptualized in Developmental Perspective: A Bioecological Model. *Psychological Review*, *101*, 568-586.

Brookstein, F. L., Connor, P. D., Huggins, J. E., Barr, H. M., Pimentel, K. D., & Streissguth, A. P. (2007). Many Infants Prenatally Exposed to High Levels of Alcohol Show One Particular Anomaly of the Corpus Callosum. *Alcoholism: Clinical and Experimental Research*, *31*(5), 868-879.

Brookstein, F. L., Streissguth, A. P., Sampson, P. D., Connor, P. D., & Barr, H. M. (2002). Corpus Callosum Shape and Neuropsychological Deficits in Adult Males with Heavy Fetal Alcohol Exposure. *Neuroimage*, *15*(1), 233-251.

Brown, R. T., Coles, C. D., Smith, I. E., Platzman, K. A., Silverstein, J., Erickson, S., & Falek, A. (1991). Effects of prenatal alcohol exposure at school age. II. attention and behavior. *Neurotoxicology and Teratology, 13*(4), 369-376.

Brunnekreef, J. A., De Sonneville, L. M. J., Althaus, M., Minderra, R. B., Oldehinkel, A. J., Verhulst, f. C., & Ormel, J. (2007). Information processing profiles of internalizing and externalizing behavior problems: evidence from a population-based sample of preadolescents. *Journal of Child Psychology and Psychiatry*, *48*(2), 185-193.

Burd, L., Klug, M. G., Martsolf, J. T., & Kerbeshian, J. (2003). Fetal alcohol syndrome: Neuropsychiatric phenomics. *Neurotoxicology and Teratology, 25*(6), 697-705.

Burden, M. J., Jacobson, S. W., Sokol, R. J., & Jacobson, J. L. (2005). Effects of prenatal alcohol exposure on attention and working memory at 7.5 years of age. *Alcoholism: Clinical and Experimental Research*, *29*(3), 443–452.

Burden, M. J., Jacobson, J. L., Westerlund, A., Lundahl, L. H., Morrison, A., Dodge, N. C., Klorman, R., Nelson, C. A., Avison, M. J., & Jacobson, S. W. (2010). An Event-Related Potential Study of Response Inhibition in ADHD With and Without Prenatal Alcohol Exposure. *Alcoholism: Clinical and Experimental Research*, *34*(4), 617-27.

Burke, N. J., Hellman, J. L., Scott, B. G., Weems, C. F., Carrio, V. G. (2011). The impact of adverse childhood experiences on an urban pediatric population. *Child Abuse & Neglect*, 35 (6), 408-413. doi:10.1016/j.chiabu.2011.02.006

Carmichael-Olson, H., Rosalind, O., Gelo, J. & Beck, S. (2009). "Family Matters:" Fetal Alcohol Spectrum Disorders and The Family. *Developmental Disabilities Research Reviews*, *15*, 235-249.

Carmichael Olson, H., Streissguth, A. P., Sampson, P. D., Barr, H. M., Bookstein, F. L., & Thiede, K. (1997). Association of prenatal alcohol exposure with behavioral and learning problems in early adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1187–1194.

Caron, C., & Rutter, M. (1991). Comorbidity in child psychopathology: Concepts, issues and research strategies. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 32*(7), 1063-1080.

Casey, B. J., Tottenham, N., Liston, C., & Durston, S. (2005). Imaging the developing brain: What have we learned about cognitive development? *Trends in Cognitive Sciences, 9*(3), 104-110. doi: 10.1016/j.tics.2005.01.011

Caspers, K. M., Oltean, C., Romitti, P. A., Sun, L., Pober, B. R., Rasmussen, S. A., & National Birth Defects Prevention Study. (2010). Maternal periconceptional exposure to cigarette smoking and alcohol consumption and congenital diaphragmatic hernia. *Birth Defects Research. Part A, Clinical and Molecular Teratology, 88*(12), 1040-1049. doi: 10.1002/bdra.20716; 10.1002/bdra.20716

Champagne, F. A., & Curley, J. P. (2009). Epigenetic mechanisms mediating the long-term effects of maternal care on development. *Neuroscience and Biobehavioral Reviews*, *33*, 593-600.

Chapman, D. P., Dube, S. R., Anda, R. F. (2007). Adverse Childhood Events as Risk Factors for Negative Mental Health Outcomes. *Psychiatric Annals*, *37*(5), 359-364.

Chapman, D. P., Liu, Y., Preley-Cantreil, L. R., Edwards, V. J., Wheaton, A. G., Perry, G. S., & Croft, J. B. (2009). Adverse childhood experiences and frequent insufficient sleep in 5 U.S. States, 2009: a retrospective cohort study. *BMC Public Health*, *13*(3) 1-9.

Chapman, D. P., Wheaton, A. G., Anda, R. F., Croft, J. B., Edwards, V. J., Liu, Y. Sturgis, S. L., & Perry, G. S. *Adverse Childhood Experiences and Sleep Disturbances in Adults*, *12*(8), 773-779.

Chasnoff, I. J., Wells, A. M. & King, L. (2015). Misdiagnosis and Missed Diagnoses in Foster and Adoptive Children with Prenatal Alcohol Exposure. *Pediatrics*, *135*(2), 264-270. doi: 10.1542/peds.2014-2171

Chiodo, L. M., Janisse, J., Delaney-Black, V., Sokol, R. J., & Hannigan, J. H. (2009). A metric of maternal prenatal risk drinking predicts neurobehavioral outcomes in preschool children. *Alcoholism, Clinical and Experimental Research, 33*(4), 634-644. doi: 10.1111/j.1530-0277.2008.00878.x

Chudley, A. E., Conry, J., Cook, J. L., Loock, C., Rosales, T., LeBlanc, N., & Public Health Agency of Canada's National Advisory Committee on Fetal Alcohol Spectrum Disorder. (2005). Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ: Canadian Medical Association Journal, 172*(5), S1-S21. doi: 10.1503/cmaj.1040302

Clark, L., Chamberlain, S. R., & Sahakian, B. J. (2009). Neurocognitive mechanisms in depression: implications for treatment. *Annual Review of Neuroscience*, *32*, 57-74.

Clarren, S. K., & Smith, D. W. (1978). The fetal alcohol syndrome. *The New England Journal of Medicine, 298*(19), 1063-1067. doi: 10.1056/NEJM197805112981906

Conners, C. K. & MHS Staff, (2000). *Conners' Continuous Performance Test II:*

Computer Program for Windows Technical Guide and Software Manual. North Tonawanda, NY: Multi-Health Systems.

Costello, E. J., Mustillo, S., Erkanli, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry*. *60*(8), 837– 844.

Coles, C., Kable, J., Taddeo, E., & Strickland, D. C. (2015). A metacognitive strategy for reducing disruptive behavior in Children with Fetal Alcohol Spectrum Disorders: GoFAR Pilot. *Alcoholism: Clinical and Experimental Research*, *39*(11), 2224-2233, DOI: 10.1111/acer.12885.

Coles, C. D., Platzman, K. A., Lynch, M. E., & Freides, D. (2002). Auditory and Visual Sustained Attention in Adolescents Prenatally Exposed to Alcohol. *Alcoholism: Clinical and Experimental Research*, *26*(2), 263-271.

Coles, C. D., Platzman, K. A., Raskind-Hood, C. L., Brown, R. T., Falek, A., Smith, I. E. (1997). A Comparison of Children Affected by Prenatal Alcohol Exposure and Attention Deficit, Hyperactivity Disorder. *Alcoholism: Clinical and Experimental Research*, *21*(1), 150-161.

Coyne, K. L., de Costa, C. M., Heazlewood, R. J., & Newman, H. C. (2008). Pregnancy characteristics of women giving birth to children with fetal alcohol syndrome in far north Queensland. *The Australian & New Zealand Journal of Obstetrics & Gynaecology, 48*(3), 240-247. doi: 10.1111/j.1479-828X.2008.00861.x

Crocker, N., Vaurio, L., Riley, E. P., & Mattson, S. N. (2009). Comparison of adaptive behavior in children with heavy prenatal alcohol exposure or attention-deficit/hyperactivity disorder. *Alcoholism: Clinical and Experimental Research*, *33*(11), 2015–2023.

Crocker, N., Vaurio, L., Riley, E. P., & Mattson, S. N. (2011). Comparison of verbal learning

and memory in children with heavy prenatal alcohol exposure or attention-deficit/hyperactivity disorder. *Alcoholism, Clinical and Experimental Research, 35*(6), 1114-1121. doi: 10.1111/j.1530-0277.2011.01444.x; 10.1111/j.1530-0277.2011.01444.x

Crowther, C.A., Doyle, L.W., Haslam, R.R., Hiller, J.E., Harding, J.E., & Robinson, J.S. (2007). Outcomes at 2 years of age after repeat doses of antenatal corticosteroids. *New England Journal of Medicine*, *357*, 1179–1189.

Damasio, A. R. (1994). Descartes' error and the future of human life. *Scientific American, 271*(4), 144.

Davis, J. C., Marra, C. A., Najafzadeh, M., & Lui-Ambrose, T. (2010). The independent contribution of executive functions to health related quality of life in older women. *BMC Geriatrics*. *10*, 16–23.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan executive function system*. San Antonio, TX: The Psychological Corporation.

Delis, D. C., Kramer, J. H., Kaplan, E., & Holdnack, J. (2004). Reliability and Validity of the Delis Kaplan Executive Function System: An update. *Journal of the International Neuropsychological Soceity*, *10*, 301-303.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1994). *Manual for the California Verbal Learning Test-Children's Version*. San Antonio, TX: The Psychological Corporation.

Denys, K., Zwaigenbaum, L., Andrew, G., Tough, S., & Rasmussen, C. (September, 2011). *Executive Functioning Predicts Adaptive Functioning in Children and Adolescents with FASD and PAE*. Presented at Fetal Alcohol Canadian Expertise (FACE), Prince Edward Island, Canada.

Denson, T. F., Pederson, W. C., Friese, M., Hahm, A., & Roberts, L. (2011). Understanding impulsive aggression: Angry rumination and reduced self-control capacity are mechanisms underlying the provocation-aggression relationship. *Personality and Social Psychology Bulletin*, *37*, 850–62.

Di Trani, M., Casini, M. P., Capuzzo, F., Gentile, S., Bianco, G., Menghini, D., & Vicari, S. (2011). Executive and intellectual functions in attention-deficit/hyperactivity disorder with and without comorbidity. *Brain & Development, 33*(6), 462-469. doi: 10.1016/j.braindev.2010.06.002

Diamond, A. (1990a). Developmental time course in human infants and infants monkeys, and the neural bases of inhibitory control in reaching. *Annals of the New York Academy of Sciences,* 608, 637-676.

Diamond, A. (1990b). The development and neural bases of memory functions as indexed by the AB and delayed response tasks in human infants and infant moneys. *Annals of the New York Academy of Sciences*, 608, 267-317.

Diamond, A. (2002). Normal development of prefrontal cortex from birth to young adulthood: Cognitive functions, anatomy, and biochemistry. In D. T. Stuss & R. T. Knight (eds.), *Principles of frontal lobe function* (p. 466-503). London, UK: Oxford University Press.

Diamond, A. (2005). Attention-deficit disorder (attention-deficit/hyperactivity disorder without hyperactivity): a neurobiologically and behaviorally distinct disorder from attention-deficit/hyperactivity disorder (with hyperactivity). *Developmental Psychopathology*, *17*, 807–25.

Diamond, A. (2006). The early development of executive functions. *Lifespan Cognition: Mechanisms of Change. pp. 70-95.*(E. Bialystok & F. Craik [(eds.]). NYC, NY: Oxford

University Press.

Diamond, A. (2009). The Interplay of Biology and the Environment Broadly Defined. *Developmental Psychology*, *45*(1), 1-8. doi:10.1037/a0014601

Diamond, A. (2012). Executive Functions. *Annual Review in Psychology*, *64*, 135-68. Diamond, A., & Goldman-Rakic, P. S. (1989). Comparison of human infants and rhesus monkeys on Piaget's AB task: Evidence for dependence on dorsolateral prefrontal cortex. *Experimental Brain Research, 74*(1), 24-40.

Disney, E. R., Iacono, W., McGue, M., & Legrand, L. (2008). Strengthening the case: Prenatal alcohol exposure is associated with increased risk for conduct disorder. *Pediatrics*, *122*(6), e1225–e1230.

D'Onofrio, B. M., Van Hulle, C. A., Waldman, I. D., Rodgers, J. L., Rathouz, P. J., Lahey, B. B. (2007). Causal inferences regarding prenatal alcohol exposure and childhood externalizing problems. *Archive of General Psychiatry*, *64*, 1296–1304.

Dolan M., & Lennox, C. (2013). Col and hot executive function in conduct disordered adolescents with and without co-morbid attention deficit hyperactivity disorder: relationships with externalizing behaviours. *Psychological Medicine*, 1-10, first available online March 2013.

Dube, S. R. Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564-572.

Eaves, L. G., Silberg, J. L., & Meyer, J. M. (1997). Genetics and developmental psychopathology. II: The main effects of genes and environment on behavioral problems in the Virginia twin study of adolescent behavioral development. *Journal of Child*

Psychology and Psychiatry, *38,* 965–80.

Ehrenrecih, J. T., & Gross, A. M. (2002). Biased attentional behavior in childhood anxiety A review of theory and current empirical investigation. *Clinical Psychology Review*, 22, 991-1008.

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

Fagerlund, A., Autti-Ramo, I., Hoyme, H. E., Mattson, S. N., & Korkman, M. (2011). Risk factors for behavioural problems in foetal alcohol spectrum disorders. *Acta Paediatrica (Oslo, Norway: 1992), 100*(11), 1481-1488. doi: 10.1111/j.1651-2227.2011.02354.x; 10.1111/j.1651-2227.2011.02354.x

Fairchild, G., van Goozen, S. H. M., Stollery, S. J., Aitken, M. R. F., Savage, J., Moore, S. C. & Goodyer, I. M. (2009). Decision Making and Executive Function in Male Adolescents with Early-Onset or Adolescence-Onset Conduct Disorder and Control Subjects. *Biological Psychiatry*, *66*, 162-168.

Feinstein, A. R. (1970). The pre-therapeutic classification of co-morbidity in chronic disease. *Journal of Chronic Diseases*, *23*(7), 455-468.

Fish, E. W., Shahrokh, D., Bagot, R., Caldji, C., Bredy, T., Szyf, M., & Meaney, M. J. (2006). Epigenetic Programming of Stress Responses through Variations in Maternal Care. *Annuals of New York Academy of Sciences*, *1036*, 167-180.

Flynn, H. A., Berman, D., & Marcus, S. M. (2009). The relationship between obstetrical outcomes and alcohol use in the year prior to pregnancy. *Journal of Psychosomatic Obstetrics and Gynaecology, 30*(4), 255-261. doi: 10.3109/01674820903276446

Forbes, G. B. (1998). Clinical Utility of the Test of Variables of Attention (TOVA) in the Diagnosis of Attention-Deficit/Hyperactivity Disorder. *Journal of Clinical Psychology*, *54*, 461-476.

Fryer, S. L., McGee, C. L., Matt, G. E., Riley, E. P., & Mattson, S. N. (2007b). Evaluation of psychopathological conditions in children with heavy prenatal alcohol exposure. *Pediatrics, 119*(3), e733-41. doi: 10.1542/peds.2006-1606

Fryer, S., Tapert, S. F., Mattson, S. N., Paulus, M. P., Spadoni, A. D., Riley, E, P. (2007a). Prenatal Alcohol Exposure Affects Frontal-Striatal Bold Response During Inhibitory Control. *Alcoholism: Clinical and Experimental Research*, *31*(8), 1415-1424.

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

Gathercole, S. E., Pickering, S. J., Ambridge, B., & Wearing, H. (2004). The structure of working memory from 4 to 15 years of age. *Developmental Psychology, 40*(2), 177-190. doi:10.1037/0012-1649.40.2.177

Gioia, G. A., Gy, S. C., & Kenworthy, L. (2000). *Behavior Rating Inventory of Executive Functioning*. Lutz, FL: Psychological Assessment Resources.

Gershon, J., & Gershon, J., (2002). A Meta-Analytic Review of Gender Differences in ADHD. *Journal of Attention Disorders*, *5*(3), 143-154.

Guler, O. E., Hostinar, C. E., Frenn, K. A., Nelson, C. A., Gunnar, M. R., & Thomas, K. M. (2012). Electrophysiological evidence of altered memory processing in children experiencing early deprivation. *Developmental Science*, *15*(3), 345-358.

Goldman-Rakic, P. S. (1987). Development of cortical circuitry and cognitive function. *Child Development, 58*(3), 601-622.

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *The American Journal of Psychiatry, 160*(4), 636-645.

Gottesman, I. I., & Hanson, D. R. (2005). Human development: Biological and genetic processes. *Annual Review of Psychology, 56*, 263-286. doi: 10.1146/annurev.psych.56.091103.070208

Graziano, P. A., McNamara, J. P., Geffken, G. R., & Reid, A. M. (2011). Differentiating co-occurring behavior problems in children with ADHD: Patterns of emotional reactivity and executive functioning. *Journal of Attention Disorders,* doi: 10.1177/1087054711428741

Greenbaum, R. L., Stevens, S. A., Nash, K., Koren, G., & Rovet, J. (2009). Social cognitive and emotion processing abilities of children with fetal alcohol spectrum disorders: a comparison with attention deficit hyperactivity disorder. *Alcoholism: Clinical and Experimental Research*, *33*(10), 1656–1670.

Greenberg, L. M., & Waldman, I. D. (1993). Developmental normative data on the test of variables of attention (T.O.V.A.). Journal of Child Psychology and Psychiatry, 34(6), 1019–1030.

Griffiths, S. Y., Sherman, E. M., Slick, D. J., Lautzenhiser, A., Westerveld, M., & Zaroff, C. M. (2006). The factor structure of the CVLT-C in pediatric epilepsy, *Psychological Assessment*, 17(2), 212-7.

Guerri, C. (2002). Mechanisms involved in central nervous system dysfunctions induced by prenatal ethanol exposure. *Neurotoxicity Research, 4*(4), 327-335. doi: 10.1080/1029842021000010884

Guerri, C., Bazinet, A., & Riley, E. P. (2009). Foetal alcohol spectrum disorders and alterations in brain and behaviour. *Alcohol and Alcoholism (Oxford, Oxfordshire), 44*(2), 108-114. doi: 10.1093/alcalc/agn105

Gutman, S. A., & Nemeroff, C. B. (2003). Persistent central nervous system effects of an adverse early environment: clinical and preclinical studies. *Physiology & Behavior*, *79*, 471-478.

Guyer, A. E., McClure, E. B., Adler, A. D., Brotman, M. A., Rich, B. A., Kimes, A. S., Pine, D. S., Ernst, M., & Leibenluft, E. (2007). Specificity of facial expression labeling deficits in childhood psychopathology. *Journal of Child Psychology and Psychiatry*, *48*(9), 863-871.

Hackman, D. A., Farah, M. J., & Meaney, M. J. (2010). Socioeconomic status and the brain: mechanistic insights from human and animal research. *Science and Society*, *11*, 651-659.

Han, G., Klimes-Dougan, B., Jepsen, S., Ballard, K., Nelson, M., Houri, A., Kumra, S., & Cullen, K. (2012). Selective neurocognitive impairments in adolescents with major depressive disorder. *Journal of Adolescence*, *35*, 11-20.

Hannigan, J. H. (1996). What research with animals is telling us about alcohol-related neurodevelopmental disorder. *Pharmacology, Biochemistry, and Behavior, 55*(4), 489-499.

Hasler, G., Drevets, W. C., Manji, H. K., & Charney, D. S. (2004). Discovering endophenotypes for major depression. *Neuropsychopharmacology*, *29*, 1765-1781.

Health Canada, (2007). *Fetal alcohol spectrum disorder. It's your health*. Retrieved from

http://www.hcsc.gc.ca/iyh-vsv/alt_formats/cmcddcmc/pdf/fasd-etcaf_e.pdf

Hellemans, K. G., Sliwowska, J. H., Verma, P., & Weinberg, J. (2010). Prenatal alcohol exposure: Fetal programming and later life vulnerability to stress, depression and anxiety disorders. *Neuroscience and Biobehavioral Reviews, 34*(6), 791-807. doi: 10.1016/j.neubiorev.2009.06.004

Hellemans, K., Verma, P., Yoon, E., Yu, W., Weinberg, J., (2008). Prenatal alcohol exposure increases vulnerability to stress and anxiety-like disorders in adulthood. *Annuals of the New York Academy of Sciences*, *1144*, 154–175.

Henry, J., Sloane, M., Black-Pond, C. (2007). Neurobiology and neurodevelopmental impact of childhood traumatic stress and prenatal alcohol exposure. *Language, Speech, & Hearing Services in Schools*, *38*, 99–108.

Ingram, R. E. & Luxton, D. (2005). Vulnerability-stress models. In B. L. Hankin & J. R. Z. Abela (Eds.). Development of psychopathology: A vulnerability-stress perspective. New York: Sage

Jacobson, S. W., Chiodo, L. M., Sokol, R. J., & Jacobson, J. L. (2002). Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neurobehavioral outcome. *Pediatrics, 109*(5), 815-825.

Jacobson, S. W., Jacobson, J. L., Sokol, R. J., Martier, S. S., & Ager, J. W. (1993). Prenatal alcohol exposure and infant information processing ability. *Child Development, 64*(6), 1706-1721.

Jarrett, M. A., & Ollendick, T. H. (2008). A conceptual review of the comorbidity of attention-deficit/hyperactivity disorder and anxiety: Implications for future research and practice. *Clinical Psychology Review*, *28*, 1266-1280.

Jarrett, K. P. Riccio, C. A., & Siekierski, B. M. (2005). Assessment of Attention Deficit Hyperactivity Disorder (ADHD) Using the BASC and BRIEF. *Applied Neuropsychology*, 12(2), 83-93.

Jones, K. L., & Smith, D. W. (1975). The fetal alcohol syndrome. *Teratology, 12*(1), 1-10. doi: 10.1002/tera.1420120102

Jones, K. L., Smith, D. W., Ulleland, C. N., & Streissguth, P. (1973). Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet, 1*(7815), 1267-1271.

Jonsdottir, S., Bouma, A., Sergeant, J. A., & Scherder, E. J. (2006). Relationships between neuropsychological measures of executive function and behavioral measures of ADHD symptoms and comorbid behavior. *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists, 21*(5), 383-394. doi: 10.1016/j.acn.2006.05.003

Kerns, K. A., Audrey, D., Mateer, C. A., & Streissguth, A. P. (1997). Cognitive deficits in nonretarded adults with Fetal Alcohol Syndrome. *Journal of Learning Disabilities, 30*(6), 685-693.

Kerns, K. A., Silkos, S., Baker, L., & Ulrick. M. (2015). Emotion Recognition in Children with Fetal Alcohol Spectrum Disorders. *Child Neuropsychology,* (ahead of prnt), 1-21.

Kessler, R, C., Berglund, P., & Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national co-morbidity survey replication. *Archives of General Psychiatry*. *62*(6), 593– 602.

Kodituwakku, P. W. (2009). Neurocognitive profile in children with fetal alcohol spectrum disorders. *Developmental Disabilities Research Reviews, 15*(3), 218-224. doi: 10.1002/ddrr.73

Kodituwakku, P. W., Handmaker, N. S., Cutler, S. K., Weathersby, E. K., & Handmaker, S. D. (1995). Specific impairments in self-regulation in children exposed to alcohol prenatally. *Alcoholism: Clinical and Experimental Research*, *19*, 1558–1564.

Kodituwakku, P. W., Kalberg, W., & May, P. A. (2001). The effects of prenatal alcohol exposure on executive functioning. *Alcohol Research & Health: The Journal of the National Institute on Alcohol Abuse and Alcoholism, 25*(3), 192-198.

Kolb, B. & Wishaw, I. (2008). *Fundamentals of Human Neuropsychology*. 6th Edition.

Kooijmans, R., Scheres, A., & Oosterlaan, J. (2000). Response inhibition and measures of psychopathology: A dimensional analysis. *Child Neuropsychology*, *6*, 175–184.

Kooistra, L., Crawford, S., Gibbard, B., Ramage, B., & Kaplan, B. J. (2010). Differentiating attention deficits in children with fetal alcohol spectrumdisorder or attention-deficit-hyperactivity disorder. *Developmental Medicine and Child Neurology*, *52*(2), 205–211.

Kopen, A. M., Kalland, M., Autti-Ramo, I. (2009). Caregiving environment and socio-emotional development in foster-placed FASD-children. *Child and Youth Services Review*, *31*, 1049-1056.

Kroes, M., Kalff, A. C., Steyaert, J., Kessels, A. H. H., Feron, F. J. M., Hendricksen, J. G. M., Zeben, T., Troost, J., Jolles, J., & Vles, J. S. H. (2002). Longitudinal Community Study: Do Psychosocial Risk Factors and Child Behavior Checklist Scores at 5 Years of Age Predict Psychiatric Diagnoses at a Later Age? *Journal of American Academy in Child and Adolescent Psychiatry*, *41*(8), 1-9.

Kushe, C. A., Cook, E. T., & Greenberg M. T. (1993). Neuropsychological and Cognitive Functioning in Children with Anxiety, Externalizing, and Comorbid Psychopathology. *Journal of Child Clinical Psychology*, *22*(2), 172-195.

Lachar, D., & Gruber, C. P. (1995). *Personality Inventory for Youth (PIY) manual: Technical guide*. Los Angeles, CA: Western Psychological Services.

LaFrance, M. A., McLachlan, K., Nash, K., Andrew, G., Loock, C., Oberlander, T. F., & Rasmussen, C. (2014). Evaluation of the neurobehavioral screening tool in children with fetal alcohol spectrum disorders (FASD). *J Popul Ther Clin Pharmacol, 21*(2), e197-210.

Larkby, C. A., Goldschmidt, L., Hanusa, B. H., & Day, N. L. (2011). Prenatal alcohol exposure is associated with conduct disorder in adolescence: findings from a birth cohort. *Journal of American Academy Child and Adolescent Psychiatry,* 50(3), 262-271.

Lebel, C., Roussotte, F., Sowell, E. R. (2011). Imaging the Impact of Prenatal Alcohol Exposure on the Structure of the Developing Human Brain. *Neuropsychological Review*, *21*, 102-118.

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

Lenroot, R. K., & Giedd, J. N. (2006). Brain development in children and adolescents: Insights from anatomical magnetic resonance imaging. *Neuroscience and Biobehavioral Reviews, 30*(6), 718-729. doi: 10.1016/j.neubiorev.2006.06.001

Linnet, K. M., Dalsgaard, S., Obel, C., Wisborg, K., Henriksen, B. T., Rodriguez, A., Kotimaa, A., Moilanen, A., Thomsen, P. H., Olsen, J., Jarvelin, M-R. (2003). Maternal Lifestyle Factors in Pregnancy Risk of Attention Deficit Hyperactivity Disorder and Associated Behaviors: Review of the Current Evidence. *American Journal of Psychiatry*, *160*, 1028-1040.

Liu, D., Diorio, J., Tannenbaum, B., Caldji, C., Francis, D., Freedman, A., Sharma, S., Pearson,

D., Plotsky, P. M., & Meaney, M. J. (1997). Maternal Care, Hippocampal Glucocorticoid Receptors, and Hypothalamic-Pituitary-Adrenal Responses to Stress. *Science*, *277*, 1659-1662.

Lupien, S., Lecours, A. R., Lussier, I., Schwartz, G., Nair, N. P., & Meaney. M. J. (1994). Basal cortisol-levels and cognitive deficits in human aging. *Journal of Neuroscience*, *14*, 2893–2903.

Ma, X., Coles, C. D., Lynch, M. E., Laconte, S. M., Zurkiya, O., Wang, d., & Hu. X. (2005) Evaluation of corpus callosum anisotropy in young adults with fetal alcohol syndrome according to diffusion tensor imaging. *Alcoholism: Clinical and Experimental Research*, *29*, 1214–22.

Maclean K. (2003). The impact of institutionalization on child development. *Developmental Psychopathology, 15,* 853–84

Mana, S., Paillere-Martinot, M. L., & Martinot, J. L. (2010). Brain imaging findings in children and adolescents with mental health disorders: a cross-sectional review. *Biological Psychiatry*, *25*, 345-354.

Mattis, S., Papolos, D., Luck, D., Cockerham, M., & Thode, H. C., Jr. (2011). Neuropsychological factors differentiating treated children with pediatric bipolar disorder from those with attention-deficit/hyperactivity disorder. *Journal of Clinical and Experimental Neuropsychology, 33*(1), 74-84. doi: 10.1080/13803395.2010.493146

Mattson, S. N., Crocker, N., & Nguyen, T. T. (2011). Fetal alcohol spectrum disorders: Neuropsychological and behavioral features. *Neuropsychology Review, 21*(2), 81-101. doi:10.1007/s11065-011-9167-9

Mattson, S. N., Goodman, A. M., Caine, C., Delis, D. C., & Riley, E. P. (1999). Executive functioning in children with heavy prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 23*(11), 1808-1815.

Mattson, S. N., & Riley, E. P. (1998). A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcoholism: Clinical and Experimental Research, 22*(2), 279-294.

Mattson, S. N., & Riley, E. P. (2000). Parent ratings of behavior in children with heavy prenatal alcohol exposure and IQ-matched controls. *Alcoholism: Clinical and Experimental Research, 24*(2), 226-231.

Mattson, S. N., Riley, E. P., Delis, D. C., Stern, C., & Jones, K. L. (1996). Verbal learning and memory in children with fetal alcohol syndrome. *Alcoholism: Clinical and Experimental Research, 20*(5), 810-816.

Mattson, S. N., Fryer, S. L., McGee, C. L., & Riley, E. P. (2008). *Fetal Alcohol Syndrome*. In Nelson, C. A., & Luciana, M. (2008). Handbook of Developmental Cognitive Neuroscience, pp 643-653.

Mattson, S. N., Riley, E. P., Gramling, L., Delis, D. C., & Jones, K. L. (1997). Heavy prenatal alcohol exposure with or without physical features of fetal alcohol syndrome leads to IQ deficits. *The Journal of Pediatrics, 131*(5), 718-721.

Mattson, S. N., Riley, E. P., Gramling, L., Delis, D. C., & Jones, K. L. (1998). Neuropsychological comparison of alcohol-exposed children with or without physical features of fetal alcohol syndrome. *Neuropsychology, 12*(1), 146-153.

Mattson, S. N., Riley, E. P., Sowell, E. R., Jernigan, T. L., Sobel, D. F., & Jones, K. L. (1996). A decrease in the size of the basal ganglia in children with fetal alcohol syndrome. *Alcoholism, Clinical and Experimental Research, 20*(6), 1088-1093.

Mattson, S. N., Roesch, S. C., Glass, L., Deweese, B. N., Claire, D., Coles, J., May, W. O., Kalberg, E. R., Sowell, C. M., Kenneth, A., Lyons, J., Riley, E. P., & the CIFASD. (2012). Further Development of a Neurobehavioral Profile of Fetal Alcohol Spectrum Disorders. *Alcoholism: Clinical and Experimental Research*, *First Available Online*, 1-12.

May, P. A., Gossage, J. P., Kalberg, W. O., Robinson, L. K., Buckley, D., Manning, M., & Hoyme, H. E. (2009). Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. *Developmental Disabilities Research Reviews, 15*(3), 176-192. doi: 10.1002/ddrr.68

McGee, C. L., Schonfeld, A. M., Roebuck-Spence T. M., Riley, E. P., & Mattson, S. N. (2008a). Children with Heavy Prenatal Alcohol Exposure Demonstrate Deficits on Multiple Measures of Concept Formation. *Alcoholism: Clinical and Experimental Research*, *32*(8), 1388-1397.

McGee, C. L., Fryer, S. L., Bjorkquist, O. A., Mattson, S. N., & Riley, E. P. (2008b). Deficits in social problem solving in adolescents with prenatal exposure to alcohol. *The American Journal of Drug and Alcohol Abuse*, *34*(4), 423–431.

Merikangas, K. R., Jian-ping, H., Burstein, M., Swanson, S. A., Avenevoli, S., Cui, L., Benjet, C., Georgiades, K., & Swendsen, J. (2009). Lifetime Prevalence of Mental Disorders in US Adolescents: Results from a National Co-morbidity Study-Adolescent Supplement

(NCS-A). *Journal of American Academy of Child and Adolescent Psychiatry*, *49*(10), 980-989. doi:10.1016/j.jaac.2010.05.017989

Meyer, S. C., Carlson, G. A., Wiggs, E. A., Martinez, P. E., Ronsaville, D. S., Klimes-Dougan, B., (2004). A prospective study of the association among impaired executive functioning, childhood attentional problems, and the development of bipolar disorder. *Developmental Psychopathology*, *16*(2), 461–476.

Miyake, A., & Friedman, N. P. (2012). The nature and organization of individual differences in executive functions: Four general conclusions. *Current Directions in Psychological Science, 21*(1), 8-14. doi: 10.1177/0963721411429458

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

Moriguchi, Y., & Hiraki, K. (2009). Neural origin of cognitive shifting in young children. *Proceedings of the National Academy of Sciences of the United States of America, 106*(14), 6017-6021. doi: 10.1073/pnas.0809747106

Moriguchi, Y., & Hiraki, K. (2011). Longitudinal development of prefrontal function during early childhood. *Developmental Cognitive Neuroscience, 1*(2), 153-162. doi: 10.1016/j.dcn.2010.12.004

Morrison, F. J., Ponitz, C. C., & McClelland, M. M. (2010). *Self-regulation and academic achievement in the transition to school*. In Child Development at the Intersection of Emotion and Cognition, ed. SD Calkins, M Bell, pp. 203–24. Washington, DC: American Psychological Association.

Mottram, L., & Donders, J. (2005). Construct validity of the California Verbal Learning Test – Children's Version (CVLT-C) after pediatric traumatic brain injury. *Child Neuropsychology*, 12(3), 191-203.

Murray, E. A., O'Doherty, J. P., & Schoenbaum, G. (2007). What we know and do not know about the functions of the orbitofrontal cortex after 20 years of cross-species studies. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 27*(31), 8166-8169. doi: 10.1523/JNEUROSCI.1556-07.2007

Nash, K., Stevens, S., Greenbaum, R., Weiner, J., Gideon, K., & Rovet, J. (2014). Improving executive functioning in children with Fetal Alcohol Spectrum Disorders (FASD). *Child Neuropsychology*, *21*(2), 191-209.

Nagy, Z., Westerberg, H., & Klingberg, T. (2004). Maturation of white matter is associated with the development of cognitive functions during childhood. *Journal of Cognitive Neuroscience, 16*(7), 1227-1233. doi: 10.1162/0898929041920441

Niggs, J. T. (2005). Neuropsychologic Theory and Findings in Attention-Deficit/Hyperactivity Disorder: The State of the Field and Salient Challenges for the Coming Decade. *Biological Psychiatry*, *57*, 1424-1435.

Noland, J. S., Singer, L. T., Arendt, R. E., Minnes, S., Short, E. J., & Bearer, C. F. (2003). Executive functioning in preschool-age children prenatally exposed to alcohol, cocaine, and marijuana. *Alcoholism, Clinical and Experimental Research, 27*(4), 647-656. doi: 10.1097/01.ALC.0000060525.10536.F6

O'Connor, M. J. (2014. Mental Health Outcomes Associated with Prenatal Alcohol Exposure: Genetic and Environmental Factors. *Current Developmental Disorders Reports*, *1*, 181-188. DOI 10.1007/s40474-014-0021-7

O'Connor, M. J., & Kasari, C. (2000). Prenatal alcohol exposure and depressive features in children. *Alcoholism: Clinical and Experimental Research*, *24*(7), 1084–1092.

O'Connor, M. J., & Paley, B. (2006). The relationship of prenatal alcohol exposure and the postnatal environment to child depressive symptoms. *Journal of Pediatric Psychology, 31*(1), 50-64. doi: 10.1093/jpepsy/jsj021

O'Connor, M. J., & Paley, B. (2009). Psychiatric conditions associated with prenatal alcohol exposure. *Developmental Disabilities Research Reviews, 15*(3), 225-234. doi: 10.1002/ddrr.74

O'Connor, M. J., Sha, B., Whaley, S., Cronin, P., Gunderson, B., Graham, J. (2002). Psychiatric illness in a clinical sample of children with prenatal alcohol exposure. *American Journal of Drug and Alcohol Abuse*, *28*(4), 743-54.

O'Connor, T., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years: Report from the Avon Longitudinal Study of Parents and Children. *British Journal of Psychiatry*, *180*, 502–508.

O'Hare, E. D., Lu, L. H., Houston, S. M., Bookheimer, S. Y., Mattson, S. N., O'Connor, M. J. (2009). Altered frontal-parietal functioning during verbal working memory in children and adolescents with heavy prenatal alcohol exposure. *Human Brain Mapping*, 30(10), 3200–3208.

Olley, A., Malhim G., Sachdev, P. (2007). Memory and executive functioning in obsessive-compulsive disorder: A selective review. *Journal of Affective Disorders*, *104*, 15-23.

O'Malley, K. D., & Nanson, J. (2002). Clinical implications of a link between Fetal Alcohol Spectrum Disorder and attention-deficit hyperactivity disorder. *Canadian Journal of Psychiatry*, *47*(4), 349-354.

Oosterlaan, J., Logan, G. D., & Sergeant, J. A. (1998). Response inhibition in AD/HD, CD, comorbid AD/HD+CD, anxious and normal children: A meta-analysis of studies with the stop task. *Journal of Child Psychology and Psychiatry*, *39*, 411–426.

Oosterlaan, J. Scheres, A. & Sergeant, J. A. (2005). Which Executive Functioning Deficits Are Associated With AD/HD, ODD/CD and Comorbid AD/HD+ODD/CD? *Journal of Abnormal Child Psychology*, *33*(1), 69-85.

Orstein, T. J., Arnold, K., Manassis, K., Mendiowitz, S., Schachar, R. (2010). Neuropsychological performance in childhood OCD: A preliminary study. *Depression and Anxiety*, *27*(4), 372-380.

Paintner, A., Andrew, D. W., & Burd, L. (2012). Fetal Alcohol Spectrum Disorders – Implications for Child Neurology. *Journal of Child Neurology*, *27*, 335.

Pei, J., Denys, K., Hughes, J., & Rasmussen, C. (2011). Mental health issues in fetal alcohol spectrum disorder. *Journal of Mental Health, 20*(5), 438-448. doi: 10.3109/09638237.2011.577113

Pei, J. R., Rinaldi, C. M., Rasmussen, C., Massey,V., & Massey, D. (2008). Memory patterns of acquisition and retention of verbal and nonverbal information in children with fetal alcohol spectrum disorders. *The Canadian Journal of Clinical Pharmacology*, *15*(1), e44–56.

Pennington, B. F., & Ozonoff, S. (1996). Executive Functions and Developmental Psychopathology. *Journal of Child Psychology and Psychiatry*, *37*, 51-87.

Pennington, B. F., Willcutt, E., & Rhee, S. H. (2005). Analyzing comorbidity. *Advances in Child Development and Behavior, 33*, 263-304.

Perera, S., Crewther, D., Croft, R., Keage, H., Hermens, D., & Clark, R. C. (2012). Comorbid Externalizing Behaviour in AD/HD: Evidence for a Distinct Pathological Entity in Adolescence. *PLoS ONE*, *7*(9), e41407.

Piaget, J. P. (1964). Cognitive Development in Children: Piaget Development and Learning. *Journal of Research in Science Teaching*, *2*, 176-186.

Pine, D. S., Lissek, S., Klein, R. G., Mannuzza, S., Moulton III, J. L., Guardino, M., & Woldehawariat, G. (2004). Face-Memory and emotions: associations with major depression in children and adolescents. *Journal of Child Psychology and Psychiatry*, *45*(7), 1199-1208.

Pliszka, S. R. (2000). Patterns of psychiatric co-morbidity with attention-deficit/hyperactivity disorder. *Child and Adolescent Psychiatric Clinics of North America*, *9*(3), 525-540.

Popova, S., Lange, S., Burd, L., & Rehm, J. (2012). Health care burden and cost associated with fetal alcohol syndrome: Based on official Canadian data. *PloS One, 7*(8), e43024. doi: 10.1371/journal.pone.0043024; 10.1371/journal.pone.0043024

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

Quattlebaum, J. L., & O'Connor, M. J. (2012). Higher functioning children with prenatal alcohol exposure: Is there a specific neurocognitive profile? *Child Neuropsychology: A Journal on Normal and Abnormal Development in Childhood and Adolescence,* doi: 10.1080/09297049.2012.713466

Rakic, P., 1990. *The Neocortex: Ontogeny and Phylogeny*. Plenum Press, New York.

Raldris, T. L., Bowers, T. G., & Towsey, C. (2014). Comparisons of Intelligence and Behavior in Children with Fetal Alcohol Spectrum Disorder and ADHD. *Journal of Attention Disorders*, *18*, 1-12.

Rasmussen, C. (2005). Executive functioning and working memory in fetal alcohol spectrum disorder. *Alcoholism, Clinical and Experimental Research, 29*(8), 1359-1367.

Rasmussen, C., Benz, J., Pei, J., Andrew, G., Schuller, G., Abele-Webster, L., & Lord, L. (2010). The impact of an ADHD co-morbidity on the diagnosis of FASD. *The Canadian Journal of Clinical Pharmacology = Journal Canadien De Pharmacologie Clinique, 17*(1), e165-76.

Rasmussen, C., & Bisanz, J. (2009). Executive functioning in children with fetal alcohol spectrum disorders: Profiles and age-related differences. *Child Neuropsychology: A Journal on Normal and Abnormal Development in Childhood and Adolescence, 15*(3), 201-215. doi: 10.1080/09297040802385400

Rasmussen, C., & Bisanz, J. (2011). The relation between mathematics and working memory in young children with Fetal Alcohol Spectrum Disorders. *The Journal of Special Education, 45 (3),* 184-191.

Rasmussen, C., Kulley-Martens, K., Cui, Y., Tough, S., Zwaigenbaum, L., & Andrew, G. (2013, under review). Mental Health Issues Among Children and Adolescents with Fetal Alcohol Spectrum Disorder and Prenatal Alcohol Exposure.

Rasmussen, C., Tamana, S., Baugh, L., Andrew, G., Tough, S., & Zwaigenbaum, L. (2013). Neuropsychological impairments on the NEPSY-II among children with FASD. *Child Neuropsychology: A Journal on Normal and Abnormal Development in Childhood and*

Adolescence, 19(4), 337-349. First available online March 5, 2012. doi: 10.1080/09297049.2012.658768

Rasmussen, C., Andrew, G., Zwaigenbaum, L., & Tough, S. (2008). Neurobehavioural outcomes of children with fetal alcohol spectrum disorders: A Canadian perspective. *Paediatrics & Child Health, 13*(3), 185-191.

Rasmussen, C. & Bisanz, J. (2009). Executive functioning in children with Fetal Alcohol Spectrum Disorder: Profiles and age-related differences. *Child Neuropsychology*. *15 (3),* 201-215.

Rasmussen, C., Horne, K., & Witol, A. (2006). Neurobehavioral functioning in children with fetal alcohol spectrum disorder. *Child Neuropsychology*, *12*(6), 453–468.

Rasmussen, C. McAuley, R., & Andrew, G. (2007). Parental Ratings of Children with Fetal Alcohol Spectrum Disorder on the Behavior Rating Inventory of Executive Function (BRIEF). *Journal of FAS International*, *5*(e2), 1-8.

Rasmussen, C. (2012, September). *Mental health issues among children and adolescents with Fetal Alcohol Syndrome Disorders and Prenatal Alcohol Exposure.* 13th annual Fetal Alcohol Canadian Expertise (FACE) Research Roundtable, Saskatoon, Saskatchewan.

Reynolds, C. R., & Kamphaus, R. W. (1992). *The Behavior Assessment System of Children*. Circle Pines, MN: American Guidance Services.

Riley, E. P., Mattson, S. N., Sowell, E. R., Jernigan, T. L., Sobel, D. F., & Jones, K. L. (1995). Abnormalities of the corpus callosum in children prenatally exposed to alcohol. *Alcoholism, Clinical and Experimental Research, 19*(5), 1198-1202.

Riley, E. P., & McGee, C. L. (2005). Fetal alcohol spectrum disorders: an overview with emphasis on changes in brain and behavior. *Experimental Biology and Medicine*, *230*(6), 357-365.

Robinson, M., Oddy, W. H., Li, J., Kendall, G. E., de Klerk, N. H., Silburn, S. R., Zubrick, S. R., Newnham, J. P., Stanley, F. J., & Mattes, E. (2008). Pre- and postnatal influences on preschool mental health: a large-scale cohort study. *Journal of Child Psychology and Psychiatry*, *49*(10),1118-1128.

Robinson, M., Oddy, W. H., McLean, N. J., Jacoby, P., Pennell, C. E., & de Klerk, N. H. (2010). Low-moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study. *BJOG: An International Journal of Obsterics & Gynaecology*, *117*, 1139–50.

Roebuck, T. M., Mattson, S. N., & Riley, E. P. (1999). Behavioral and psychosocial profiles of alcohol-exposed children. *Alcoholism: Clinical and Experimental Research, 23*(6), 1070- 1076.

Roebuck, T. M., Mattson, S. N., & Riley, E. P. (2002). Interhemispheric transfer in children with heavy prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 26*(12), 1863-1871. doi: 10.1097/01.ALC.0000042219.73648.46

Rodriguez, A., Olsen, J., Kotimaa, A. J., Kaakinen, M., Moilanen, I., Henriksen, T. B. (2009). Is prenatal alcohol exposure related to inattention and hyperactivity symptoms in children? Disentangling the effects of social adversity. *Journal of Child Psychology and Psychiatry*, *50*, 1073–83.

Rommelse, N. N., Altink, M. E., Martin, N. C., Buschgens, C. J., Faraone, S. V., Buitelaar, J. K., & Oosterlaan, J. (2008). Relationship between endophenotype and phenotype in ADHD. *Behavioral and Brain Functions: BBF, 4*(4), 1-14. doi: 10.1186/1744-9081-4-4

Roth, R. H., Tam, S. Y., Ida, Y., Yang, J. X., Deutch, A. Y. (1988). Stress and the mesocorticolimbic dopamine systems. *Annals of the New York Academy of Sciences*, *537*, 138–147.

Rubia, K. (2011). "Cool" Inferior Frontostriatal Dysfunction in Attention-Deficit/Hyperactivity Disorder Versus "Hot" Ventromedial Orbitofrontal-Limbic Dysfunction in Conduct Disorder: A Review. *Biological Psychiatry*, *69*, e69-e87.

Rutter, M., Kreppner, A., & Sonuga-Barke, E. (2009). Emanuel Miller Lecture: Attachment insecurity, disinhibited attachment, and attachment disorders: where do research findings leave the concepts? *Journal of Child Psychology and Psychiatry*, *50*(5), 529-543.

Sampson, P., Streissguth, A. P., Bookstein, F., & Barr, H. (2000). On categorizations in analysis of alcohol teratogenesis. *Environmental Health Perspective*, 108, 421–428.

Sayal, K. (2007). Alcohol consumption in pregnancy as a risk factor for later mental health problems. *Evidenced Based Mental Health*, *10*(4), 98-100.

Sayal K., Heron, J., Golding, J., Alati, R., Smith, D. Gray, R., & Edmond, A. (2009). Binge Pattern of Alcohol consumption During Pregnancy and Childhood Mental Health Outcomes: Longitudinal Population-Based Study. *Pediatrics*, *123*, e289-e296.

Sayal K, Heron J, Golding J, & Emond A. (2007) Prenatal alcohol exposure and gender differences in childhood mental health problems: a longitudinal population-based study. *Pediatrics*, *19*(2): e426.

Schatz, D. B., & Rostain, A. L. (2006). ADHD with comorbid anxiety: A review of the current

literature. *Journal of Attention Disorders*, *10*, 141-149.

Schonfeld, A. M., Paley, B., Frankel, F., & O'Connor, M. J. (2006). Executive functioning predicts social skills following prenatal alcohol exposure. *Child Neuropsychology*, *12*(6), 439–452.

Semrud-Clikeman, M., & Teeter Ellison, P. A. (2009). *Child Neuropsychology: Assessment and Interventions for Neurodevelopmental Disorders*. Second Eds. Springer.

Sokol, R. J., & Clarren, S. K. (1989). Guidelines for use of terminology describing the impact of prenatal alcohol on the offspring. *Alcoholism: Clinical and Experimental Research, 13*(4), 597-598.

Sood, B., Delaney-Black, V., Covington, C., Nordstrom-Klee, B., Ager, J., Templin, T., Janisse, J., Martier, S., & Sokol, R. J. (2001). Prenatal alcohol exposure and childhood behavior age 6 to 7 years: I. dose-response effect. *Pediatrics*, *108*(2), E34.

Sokol, R. J., & Clarren, S. K. (1989). Guidelines for use of terminology describing the impact of prenatal alcohol on the offspring. *Alcoholism: Clinical and Experimental Research, 13*(4), 597-598.

Sorensen, L., Plessen, K. J., Nicholas, J., & Lundervold, A. J. (2011). Is behavioral regulation in children with ADHD aggravated by comorbid anxiety disorder? *Journal of Attention Disorders, 15*(1), 56-66. doi: 10.1177/1087054709356931

Sowell, E. R., Thompson, P. M., Peterson, B. S., Mattson, S. N., Welcome, S. E., Henkenius, A. L., Riley, e. P., Jernigan, T. L., & Toga, A. W. (2002). Mapping Cortical Gray Matter Asymmetry Patterns in Adolescents with Heavy Prenatal Alcohol Exposure. *NeuroImage*, *17*(4), 1807-1819.

Sowell, E. R., Johnson, A., Kan, E., Lu, L. H., Van Horn, J. D., Toga, a. W., O'Connor, M. J., &

Bookheimer, S. Y. (2008). Mapping White Matter Integrity and Neurobehavioral Correlates in Children with Fetal Alcohol Spectrum Disorders. *The Journal of Neuroscience*, *28*(6), 1313-1319.

Sowell, E. R., Lu, L. H., O'Hare, E. D., McCourt, S. T., Mattson, S. N., O'Connor, M. J., & Bookheimer, S. Y. (2007). Functional magnetic resonance imaging of verbal learning in children with heavy prenatal alcohol exposure. *Neuroreport*, *18*(7), 635-639.

Sowell, E. R., Jernigan, T. L., Mattson, S. N., Riley, E. P., Sobel, D. F., & Jones, K. L. (1996). Abnormal development of the cerebellar vermis in children prenatally exposed to alcohol: Size reduction in lobules I-V. *Alcoholism: Clinical and Experimental Research, 20*(1), 31-34.

Spohr, H. L., Willms, J., & Steinhausen, H. C. (1993). Prenatal alcohol exposure and long-term developmental consequences. *Lancet, 341*(8850), 907-910.

Spohr, H. L., Willms, J., & Steinhausen, H. C. (2007). Fetal alcohol spectrum disorders in young adulthood. *The Journal of Pediatrics, 150*(2), 175-9, 179.e1. doi: 10.1016/j.jpeds.2006.11.044

Stade, B., Ungar, W. J., Stevens, B., Beyen, J., & Koren, G. (2007). Cost of fetal alcohol spectrum disorder in Canada. *Canadian Family Physician: Medecin De Famille Canadien, 53*(8), 1303-1304.

Steinhausen, H. C., & Spohr, H. L. (1998). Long-term outcome of children with fetal alcohol syndrome: Psychopathology, behavior, and intelligence. *Alcoholism: Clinical and Experimental Research, 22*(2), 334-338.

Stephen, J. M., Kodituwakku, P. W., Kodituwakku, E. L., Romero, L., Peters, A. M., Sharadamma, N. M., & Coffman, B. A. (2012). Delays in auditory processing identified

in preschool children with FASD. *Alcoholism: Clinical and Experimental Research, 36*(10), 1720-1727. doi:10.1111/j.1530-0277.2012.01769.x; 10.1111/j.1530-0277.2012.01769.x

Streissguth, A. P. (2007). Offspring Effects of Prenatal Alcohol Exposure from Birth to 25 Years: The Seattle Prospective Longitudinal Study. *Journal of Clinical Psychology in Medical Settings*, *14*, 81-101.

Streissguth, A. P., Barr, H. M., & Martin, D. C. (1984). Alcohol exposure in utero and functional deficits in children during the first four years of life. *Ciba Foundation Symposium, 105*, 176-196.

Streissguth, A. P., Barr, H. M., & Sampson, P. D. (1990). Moderate prenatal alcohol exposure: effects on child IQ and learning problems at age 7 1/2 years. *Alcoholism: Clinical and Experimental Research*, *14*(5), 662–669.

Streissguth, A. P., Bookstein, F. L., Barr, H. M., Sampson, P. D., O'Malley, K., & Young, J. K. (2004). Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *Journal of Developmental and Behavioral Pediatrics: JDBP, 25*(4), 228- 238.

Streissguth, A. P., & O'Malley, K. (2000). Neuropsychiatric implications and long-term consequences of fetal alcohol spectrum disorders. *Seminars in Clinical Neuropsychiatry,5*(3), 177-190.

Streissguth, A. P., Barr, H. M., Bookstein, F. L., Sampson, P. D., & Carmichael-Olson, H. (1999). The Long-Term Neurocognitive Consequences of Prenatal Alcohol Exposure: A 14-Year Study. *Psychological Science*, *10*(3), 186-190.

Streissguth, A. P., Aase, J. M., Clarren, S. K., Randels, S. P., LaDue, R. A., & Smith, D. F. (1991). Fetal Alcohol Syndrome in Adolescents and Adults. *The Journal of the American*

Medical Association, *265*(15), 1961-1967.

Stuss, D. T., & Knight, R. T. (2012). *Principles of Frontal Lobe Function*. Oxford University Press: Second Eds.

Sulik, K. K. (2005). Genesis of alcohol-induced craniofacial dysmorphism. *Experimental biology and Medicine*, *230*(6), 366-375.

Szyf, M. (2009). Early life, the epigenome and human health. *Acta Paediatrica (Oslo, Norway: 1992), 98*(7), 1082-1084. doi: 10.1111/j.1651-2227.2009.01382.x .

Tamnes, C. K., Ostby, Y., Walhovd, K. B., Westlye, L. T., Due-Tonnessen, P., & Fjell, A. M. (2010). Intellectual abilities and white matter microstructure in development: A diffusion tensor imaging study. *Human Brain Mapping, 31*(10), 1609-1625. doi: 10.1002/hbm.20962

Tamana, S., Pei, J., Massey, D., Massey, V., & Rasmussen, C. (2012). Neuropsychological Impairments and Age-Related Differences in Children and Adolescents with Fetal Alcohol Spectrum Disorder. Presented at the 5th Biennial Conference on Adolescents and Adults with FASD, Vancouver, Canada.

Taylor-Tavares, J. V., Clark, L., Cannon, D. M., Erickson, K., Drevets, W. C., & Sahakian, B. J. (2007). Distinct profiles of neurocognitive function in unmedicated unipolar depression and bipolar II depression. *Biological Psychiatry*, *62*, 917–24

Thapar, A., Collishaw, S., Pine, D. S., & Thapar, A. K. (2012). Depression in adolescence. *Lancert*, *379*, 1056-57.

Uecker, A., & Nadel, L. (1996). Spatial locations gone awry: object and spatial memory deficits in children with fetal alcohol syndrome. *Neuropsychologia*, *34*(3), 209–223.

Van Waes, V., Enache, M., Berton, O., Vinner, E., Lhermitte, M., Maccarim, S., & Darnaudery,

M. (2010). Effect of prenatal stress on alcohol preference and sensitivity to chronic alcohol exposure in male rats. *Psychopharmacology*, *214*, 197-208.

Vaurio, L., Riley, E. P., & Mattson, S. N. (2008). Differences in executive functioning in children with heavy prenatal alcohol exposure or attention-deficit/hyperactivity disorder. *Journal of the International Neuropsychological Society*, *14*, 119–129

Vaurio, L., Riley, E. P., & Mattson, S. N. (2011). Comparison of neuropsychological performance in children with heavy prenatal alcohol exposure and an IQ-matched comparison group. *Journal of* the *International Neuropsychological Society*. *17*, 463-473.

Vestergaard, M., Madsen, K. S., Baare, W. F., Skimminge, A., Ejersbo, L. R., Ramsoy, T. Z., & Jernigan, T. L. (2011). White matter microstructure in superior longitudinal fasciculus associated with spatial working memory performance in children. *Journal of Cognitive Neuroscience, 23*(9), 2135-2146. doi: 10.1162/jocn.2010.21592

Vinnerljung, B., & Sallna, M. (2008). Into adulthood: a follow-up study of 718 young people who were placed in out-of-home care during their teens. *Child and Family Social Work*, *13*,144–55.

Viguera, A. C., Tondon, L., Koukopoulos, A. E., Reginaldi, M. D., Lepri, B., & Baldessarini, R. J., (2011). Episodes of Mood Disorders in 2,252 Pregnancies and Postpartum Periods. *The American Journal of Psychiatry*, *168*, 1179-1185. Doi. 10.1176/appi.ajp.2011.11010148

Waddell, C., Offord, D. R., Shepherd, C. A., Hua, J. M., & McEwan, K. (2002). Child psychiatric epidemiology and Canadian public policy-making: the state of the science and the art of the possible. *Canadian Journal of Psychiatry*, *47*(9), 825-832.

Walthall, J., O'Connor, M., & Paley, B. (2008). A comparison of psychopathology in children

with and without prenatal alcohol exposure. *Mental Health Aspects of Developmental Disabilities*, *11*, 69–78.

Ware, A. L., Crocker, N., O'Brien, J. W., Deweese, B. N., Roesch, S. C., Coles, c. D., Kable, J. A., May, P. A., Kalberg, K. O., Sowell, E. R., Jones, K. L., Riley, E. P., Mattson, S. N., & CIFASD (2012a) Executive function predicts adaptive behavior in children with histories of heavy prenatal alcohol exposure and attention-deficit/hyperactivity disorder. *Alcoholism: Clinical and Experimental Research*, *36*(8), 1431-41.

Ware, A. L., O'Brien, J. W., Crocker, N., Deweese, B. N., Roesch, S. C., Coles, C. D., Kable, J. A., May, P. A., Kalberg, W. O., Sowell, E. R., Jones, K. L., Riley, E. P., & Mattson, S. N. (2012b). The Effects of Prenatal Alcohol Exposure and Attention-Deficit/Hyperactivity Disorder on Psychopathology and Behavior. *Alcoholism: Clinical and Experimental Research*, *37*(3), 507- 516.

Weinberg, J. (1989). Prenatal Alcohol Exposure Alters Adrenocortical Development of Offspring. *Alcoholism: Clinical and Experimental Research*, *13*(1), 73-83.

Welberg, L. A. M., & Seckl, J. R. (2001). Prenatal Stress, Glucocorticoids and the Programming of the Brain. *Journal of Neuroendocrinology, 13*, 113-128.

Welberg, L. A. M., Seckl, J. R., & Holmes, M. C. (2001) Prenatal Glucorcoticoid Programming of Brain Corticosteroid Receptors and Corticotrophin-Releasing Hormone: Possible Implications for Behaviour. *Neuroscience*, *104*(1), 71-79.

Welsh, M. C., & Pennington, B. F. (1988). Assessing frontal lobe functioning in children: Views from developmental psychology. *Developmental Neuropsychology*, *4*, 131–149.

Welsh & Pennington (1991). A normative-developmental study of executive function: A window on prefrontal function in children. *Developmental Neuropsychology*, *7*(2), 131-149.

Wengel, T., Hanlon-Dearman, A. C., & Fjeldsted, B. (2011). Sleep and sensory characteristics in young children with Fetal Alcohol Spectrum Disorder. *Journal of Developmental and Behavioral Pediatrics, 32*(5), 384-392.

Whaley, S. E., O'Connor, M. J., & Gunderson, B. (2001). Comparison of the adaptive functioning of children prenatally exposed to alcohol to a non-exposed clinical sample. *Alcoholism: Clinical and Experimental Research*, *25*(7), 1018–1024.

Wheeler, S. N., Stevens, S. A., Sheard, E. D., & Rovet, J. F. (2012). Facial memory deficits in children with fetal alcohol spectrum disorders. *Child Neuropsychology*, *18*(4), 339-46.

Willcutt, E.G., Doyle, A.E., Nigg, J.T., Stephen, V., Faraone, S.V., & Pennington, B.F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336–1346

Wiebe, S. A., Espy, K. A., & Charak, D. (2008). Using confirmatory factor analysis to understand executive control in preschool children: I. latent structure. *Developmental Psychology, 44*(2), 575-587. doi: 10.1037/0012-1649.44.2.575

Wiebe, S. A., Sheffield, T., Nelson, J. M., Clark, C. A., Chevalier, N., & Espy, K. A. (2011). The structure of executive function in 3-year-olds. *Journal of Experimental Child Psychology, 108*(3), 436-452. doi: 10.1016/j.jecp.2010.08.008

Willoughby, M. T., Blair, C. B., Wirth, R. J., & Greenberg, M. (2010). The measurement of executive function at age 3 years: Psychometric properties and criterion validity of a new battery of tasks. *Psychological Assessment, 22*(2), 306-317. doi: 10.1037/a0018708

Willoughby, M. T., Wirth, R. J., & Blair, C. B. (2011). Contributions of modern measurement theory to measuring executive function in early childhood: An empirical demonstration.

Journal of Experimental Child Psychology, 108(3), 414-435. doi: 10.1016/j.jecp.2010.04.007

Wirt, R. D., Lachar, D., Klinedinst, J. K., Seat, P. D., & Broen, W. E. (2001). *Multidimensional Description of Child Personality: A Manual for the Personality Inventory for Children - Second Edition*. Western Psychological Services, Los Angeles.

Wozniak, J. R., Mueller, B. A., Muetzel, R. L., Bell, C. J., Hoecker, H. L., Nelson, M. L., & Lim, K. O. (2011). Inter-hemispheric functional connectivity disruption in children with prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 35*(5), 849-861. doi: 10.1111/j.1530-0277.2010.01415.x; 10.1111/j.1530-0277.2010.01415.x

Wozniak, J. R., & Muetzel, R. L. (2011). What does diffusion tensor imaging reveal about the brain and cognition in fetal alcohol spectrum disorders? *Neuropsychology Review, 21*(2), 133-147. doi: 10.1007/s11065-011-9162-1

Wozniak, J. R., Muetzel, R. L., Mueller, B. A., McGee, C. L., Freerks, E. E., Ward, M. L., Nelson, P. C., & Kelvin, O. L. Microstructural Corpus Callosum Anomalies in Children with Prenatal Alcohol Exposure: An Extension of Previous Diffusion Tensor Imaging Findings. *Alcoholism: Clinical and Experimental Research*, *33*(10), 1-20.

Zhang, X., Sliwowska, J. H., & Weinberg, J. (2005). Prenatal alcohol exposure and fetal programming: effects on neuroendocrine and immune function. *Experimental Biology and Medicine, 230*, 376-388.

Zeanah, C. H., Boris, N. W., & Larrieu, j. A. (1996). Infant Development and Developmental Risk: A Review of the Past 10 Years. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(2), 165-178.

Zelazo, P. D. (2006). The Dimensional Change Card Sort (DCCS): a method of assessing

executive function in children, *Nature Protocols*, *1*, 297-301.

Zelazo, P. D., Carlson, S. M., & Kesek, A. (2008). *The development of executive function in childhood*. I*n* Nelson, C. & Luciana, M. (Eds), Handbook of Developmental Cognitive Neuroscience (2nd Ed.) (pp. 553–574). Cambridge, MA: MIT Press.

Zelazo, P. D., & Muller. U. (2002) *Executive function in typical and atypical development*. *In* Goswami, U. Blackwell Handbook of Childhood Cognitive Development (Eds). pp. 445–470. Blackwell Publishers Ltd., Malden, MA.

Zuckerman, M. (1999). *Vulnerability to psychopathology: A biosocial model*. Washington, DC: American Psychological Association.

Appendix A

Child Information:

ID:_____
Date of birth (mm/dd/yyyy):_____
Sex: M F
Ethnicity:_____
Does the child have a sibling with FASD or PAE? ☐ Yes ☐ No
How many? _____
Date of birth (mm/dd/yyyy):_____
Sex: M F
Ethnicity:_____
Relationship: ☐ Full ☐ Half ☐ Step
ID# in study:_____

Diagnostic Info:

Reason for referral:_____
_____
Date of assessment (mm/dd/yyyy):_____
Is this a re-assessment? Y N
Age at assessment: _____
Specific diagnosis (ie. ARND, pFAS, etc.): _____
Diagnostic code:_ _____ _____ _____
Prenatal score:_____
Postnatal score:_____
Child's FSIQ _____ percentile: _____Classification_____
Other diagnoses rendered
List all co-morbid diagnoses made *at the time of* FASD assessment *only*. Attach a blind copy of the summary page.
1._____ 3._____
2._____ 4._____

Mental Health Co-morbidities

Child has an internalizing disorder ☐ Yes ☐ No
Child has an externalizing disorder ☐ Yes ☐ No
Child has both ☐ Yes ☐ No

Check all internalizing mental health co-morbidities diagnosed when assessed for FASD:

☐ **ADHD**	☐ **ODD**	☐ **Conduct Disorder**	☐ **Substance Use Disorder**
Inattentive type			
Hyperactive type			
Combined type			
Part of FASD phenotype?	Part of FASD phenotype?	Part of FASD phenotype?	
☐ Yes ☐ No ☐ DK	☐ Yes ☐ No ☐ DK	☐ Yes ☐ No ☐ DK	
☐ New	☐ New	☐ New	☐ New
☐ Previous confirmed (upheld)	☐ Previous confirmed (upheld)	☐ Previous confirmed (upheld)	☐ Previous confirmed (upheld)
☐ At-risk (emerging)	☐ At-risk (emerging)	☐ At-risk (emerging)	☐ At-risk (emerging)
Age at diagnosis:	Age at diagnosis:	Age at diagnosis:	

Age at diagnosis:

Check all internalizing mental health co-morbidities diagnosed when assessed for FASD:

☐ **Depression**	☐ **Bipolar Disorder**	☐ **Anxiety Disorder**	☐ **Anxiety related disorder**
Major Depressive Disorder Dysthymic Disorder Not specified		Generalized (GAD) Separation Anxiety Not specified Other (i.e. social, phobia, panic etc.)	Post Traumatic (PTSD) Obsessive Compulsive (OCD)
☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:	☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:	☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:	

Please check all other psychiatric or mental health issues diagnosed when assessed for FASD:

☐ **Psychosis**	☐ **Personality**	☐ **Other Trauma/ Stress-related disorder**
Psychosis Schizophrenia Other (please specify)	Borderline Personality Disorder Other (please specify)	Adjustment disorder Acute Stress Disorder Attachment Reactive Attachment Disorder (RAD) FASD diagnosis compounded by Trauma Other (please specify)
☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:	☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:	☐ New ☐ Previous confirmed (upheld) ☐ At-risk (emerging) Age at diagnosis:

Maternal Mental Health History:

Internalizing Issues	☐ Yes	☐ No
Externalizing Issues	☐ Yes	☐ No
Both	☐ Yes	☐ No
Unknown	☐ Yes	☐ No

Please specify:

_____

_____

_____

Learning difficulties	☐ Yes	☐ No
FASD	☐ Yes	☐ No
ADHD	☐ Yes	☐ No
Substance use problems	☐ Yes	☐ No

Trouble with the law: ☐ Yes ☐ No

Medical condition _____

Paternal Mental Health History:

Internalizing Issues ☐ Yes ☐ No

Externalizing Issues ☐ Yes ☐ No

Both ☐ Yes ☐ No

Unknown ☐ Yes ☐ No

Please specify:

_____

_____

_____

Learning difficulties ☐ Yes ☐ No

FASD ☐ Yes ☐ No

ADHD ☐ Yes ☐ No

Substance use problems ☐ Yes ☐ No

Trouble with the law: ☐ Yes ☐ No

Medical condition _____

Treatment History:

Has the child ever been prescribed any medications: ☐ Yes ☐ No

If yes, please check those that apply:

Ritalin ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Dexedrine: ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Cylert: ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Antidepressants: ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Tranquilizers: ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Anticonvulsants: ☐ Yes ☐ No Mg_____ Age _____
Reason _____

Recommended at time of FASD assessment: ☐ Yes ☐ No

Other (specify): _____

Any of the meds listed above discontinued: ☐ Yes ☐ No Please Specify

_____

Postnatal info:

Demographic Information:

Highest maternal education (bio mother):

Elementary school or less	Partial high school
Junior high school	High school graduate
Partial university or trade school	University graduate
Graduate degree	Other: please specify:

Bio Mothers Ethnicity:_____

Bio Father's Ethnicity:_____

Living arrangement/primary caregiver at time of assessment:

☐ Single parent ☐ Both parents

Biological parent(s)	Non-adoptive relative(s)	Grandparent(s)
Adoptive parent(s)	Shared living/group home	Other (please specify):
Foster parent(s)	Respite care	
Adoptive relatives	Friends/family friends	

Occupation of primary caregiver_____

Who has custody of the child (if different than primary caregiver)?_____

Time in current residence_____

Number of different living arrangements up to time of assessment:_____

Indicate types of living arrangements up until time of assessment (i.e. bio parents until age 3, then 2 foster placements)

_____

_____

_____

_____

_____

Multiple Moves: ☐ Yes ☐ No ☐ Suspected ☐ DK

Type of care: _____

Length of time with foster or adoptive parents: _____

Length of time with biological parents: _____

Length of time in group home: _____

Postnatal Experiences:

Childhood accident or head injury: ☐ Yes ☐ No ☐ Suspected ☐ DK (Please specify):

_____

_____

Lack of early childhood stimulation: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

History of Neglect: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

_____

History of Abandonment: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

History of traumatic events or experiences: ☐ Yes ☐ No ☐ Suspected ☐ DK

Major Life Event ☐ Yes ☐ No ☐ Suspected ☐ DK
List all major changes in circumstance (e.g. divorce, bereavement) _____

Change in caregiver relationship status: ☐ Yes ☐ No ☐ DK

Caregiver health or mental health problem: ☐ Yes ☐ No ☐ DK

Caregiver medication: ☐ Yes ☐ No ☐ DK

Any other relevant information:

Postnatal Environment:

History of emotional abuse toward child: ☐ Yes ☐ No ☐ Suspected ☐ DK

History of physical abuse toward child: ☐ Yes ☐ No ☐ Suspected ☐ DK

History of sexual abuse toward child: ☐ Yes ☐ No ☐ Suspected ☐ DK

Exposure to family violence in home: ☐ Yes ☐ No ☐ Suspected ☐ DK

History of unstable home environment: ☐ Yes ☐ No ☐ Suspected ☐ DK

History of drug/alcohol abuse in child's living situation ☐ Yes ☐ No ☐ Suspected ☐ DK

Prenatal information:

Alcohol History:

Alcohol consumption of the birth mother:

Before Pregnancy

Average # of drinks per drinking occasion: _____
Maximum # of drinks per drinking occasion: _____
Average number of drinking days per week: _____
Type of Alcohol: ☐ wine ☐ beer ☐ liquor ☐ DK ☐ other_____

During Pregnancy

Average # of drinks per drinking occasion: _____
Maximum # of drinks per drinking occasion: _____

Average number of drinking days per week: _____

Type of Alcohol: ☐ wine ☐ beer ☐ liquor ☐ unknown ☐ other_____

Trimester(s) in which consumed: ☐ 1st ☐ 2nd ☐ 3rd ☐ DK ☐ none

Was the birth mother ever diagnosed with alcoholism? ☐ Yes ☐ Suspected ☐ No ☐ DK

Was the birth mother ever reported to have a problem with alcohol? ☐ Yes ☐ Suspected ☐ No ☐ DK

Did the birth mother ever receive treatment for alcohol addiction? ☐ Yes ☐ Suspected ☐ No ☐ DK

Was alcohol use during this pregnancy positively confirmed? ☐ Yes ☐ Suspected ☐ No ☐ Unknown

If yes, what was the source? ☐ Birth mother ☐ Direct observer ☐ Individual/source that didn't directly observe drinking ☐ Missing

Reported use of alcohol during pregnancy is: ☐ Reliable ☐ Questionable ☐ Unknown ☐ Missing

At what age did the birth mother start drinking? _____

Exposure to other substances: ☐ Yes ☐ No ☐ Suspected ☐ DK

Please specify: ☐ Cigarettes ☐ Marijuana ☐ Amphetamines ☐ Cocaine ☐ Heroine ☐ PCP ☐ Crystal Meth ☐ Prescription Meds _____ ☐ Other: _____

Prenatal Factors During Pregnancy:

Poor prenatal care: ☐ Yes ☐ No ☐ Suspected ☐ DK

Number of antenatal visits: _____

Pregnancy complications: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

Prescribed medications: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

Maternal medical condition (i.e. Diabetes, epilepsy, HIV, infection): ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

Maternal stress (i.e. chronic stress, trauma, exposure to violence etc.) ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

Maternal mental health concerns: ☐ Yes ☐ No ☐ Suspected ☐ DK

_____

List all major changes in circumstance during pregnancy (e.g. divorce/separation, bereavement)

_____

_____

Prenatal Factors At-Birth:

Maternal age at birth:

Apgar Score:

Length of pregnancy: _____

Gestational weight: _____

Gestational size: _____

Head circumference: _____

Type of delivery: _____

Para: _____

Gravity: _____

Prematurity ☐ Yes ☐ No ☐ Suspected ☐ DK

Neonatal Abstinence Syndrome (NAS) ☐ Yes ☐ No ☐ Suspected ☐ DK

Emergency Medication Intervention (I.e. ICU care) ☐ Yes ☐ No ☐ Suspected ☐ DK

Perinatal complications (e.g. head injury, stroke) ☐ Yes ☐ No ☐ Suspected ☐ DK

Seizures/convulsions: ☐ Yes ☐ No ☐ Suspected ☐ DK

Other concerns at birth: ☐ Jaundice Infection ☐ Low HR ☐ Lack of Oxygen ☐ Feeding problems

List any additional relevant information:

_____
_____
_____
_____

Appendix B

Study Variables

Coding

Primary outcome variables

Main predictor variables were coded as dichotomous (yes/no) outcomes. Both internalizing disorder and externalizing disorder were coded as yes = 1 and no = 0.

Secondary outcome variables

Other variables were coded as dichomous or continuous variables. Mental health diagnosis and mental health issue were coded as confirmed = 1, no = 0; total number of mental health diagnoses were coded as a continuous variable ranging from 0 to 5; and type of disorder were coded as yes or at risk = 1, no = 0.

Predictor variables

Various demographic, diagnostic, and prenatal and postnatal factors were coded as dichotomous variables, 0 = no, 1 = yes or suspected, with the exception of factors ranging on a scale (categorical predictors variables) and factors represented by a score (continous predictor variables).

Categorical predictor variables included prenatal and posnatal score (0 =no risk to 4 = high risk); ACE score (0= no ACEs endorsed to 10 = ten ACEs endorsed); FASD diagnosis (FAS = 4 to Neurobehavioral disorder =1 or PAE = 0); intellectual ability (0 = borderline to high average = 4); maternal education (0 = less than junior high to 4 = postsecondary or university); and living situation (0 = biological home to 3 = fostercare or other = 4).

Continuous predicator variables included maternal age, gestational age, gestational weight, gravida, para, apgar score, number of placements, number of medications.

Primary outcome variables

a) *Externalizing disorder*: Child identified as have attention deficit hyperactivity disorder, oppositional defiant disorder, and/or conduct disorder based clinical diagnosis made or confirmed by the FASD clinical team.

b) *Internalizing disorder*: Child identified as have anxiety disorder, depression, post traumatic stress disorder, attachment disorder, and/or reactive attachment disorder based clinical diagnosis made or confirmed by the FASD clinical team.

Secondary outcome variables

a) *Mental health diagnosis*: child diagnosed with a mental health disorder, extracted from clinical file.

a) *Mental health issue*: Child identified as at-risk for developing a mental health disorder, extracted from clinical file.

b) *Total number of mental health co-morbidities*: Total number of diagnoses made or confirmed at the time of FASD assessment

c) *Attention Deficit Hyperactivity Disorder (ADHD)*: Child diagnosed or at-risk for ADHD, as confirmed by clinical file.

d) *Oppositional Defiant Disorder (ODD) or Conduct disorder*: Child diagnosed or at-risk for ODD or Conduct Disorder, as confirmed by clinical file.

e) *Anxiety disorder*: Child diagnosed or at-risk for generalized anxiety disorder, obsessive compulsive disorder, anxiety not specified, as confirmed by clinical file.

f) *Depression*: Child diagnosed or at-risk for dysthimia, major depressive disorder, depression not specified, as confirmed by clinical file.

g) Post Traumatic Stress Disorder (PTSD): Child diagnosed or at-risk for PTSD, as confirmed by clinical file.

h) Other mental health problem: Child diagnosed or at-risk for severe psychiatric issue, as confirmed by clinical file.

Predicator variables/confounders

Child characteristics

a) *Age in years*: Child age at assessment was extracted from clinical file.

b) *Gender*: Child identified as male or female based on clinical file.

c) *Intellectual ability*: IQ score classifications, ranging from borderline to high average, extracted from clinical files. Intellectual ability was grouped into a binary variable: 0 = below borderline range and 1 = above borderline range.

Child FASD diagnosis

a) *FASD or PAE*: Child has Fetal Alcohol Spectrum Disorder (FASD) or confirmed prenatal alcohol exposure (PAE) but did not criteria for an FASD diagnosis, extracted from clinical file.

b) *FASD Diagnosis*: Child met criteria for fetal alcohol syndrome (FASD); partial fetal alcohol syndrome (pFAS); static encephalopathy: alcohol exposed; and neurobehavioral disorder: alcohol exposed; or neurobehavioral disorder: alcohol exposed not FASD (PAE).

c) *Postnatal score*: prenatal factors ranked as part of the FASD diagnostic assessment to describe relative risk ranging from 0 (unknown), 1 (no risk), 2 (some risk), 4 (high risk), extracted from clinical file.

d) *Prenatal score*: postnatal factors ranked as part of the FASD diagnostic assessment to describe relative risk ranging from 0 (unknown), 1 (no risk), 2 (some risk), 4 (high risk), extracted from clinical file.

Family Characterisitcs

a) *Biological parent mental health*: Families completed an intake form at the time of their FASD assessment. Maternal and paternal history of emotional, behavioral, FASD, ADHD, learning problems, or psychiatric disorder were extracted from clinical file. Information was reported as yes or suspected history of mental health issues.

b) *Substance use problems*: Maternal and paternal history drug and alcohol misuse were extracted from an intake form completed at the time of their FASD assessment. Information was reported as yes or suspected.

c) *Trouble with the law*: Maternal and paternal legal problems were extracted from an intake form completed at the time of their FASD assessment. Information was reported as yes or suspected or suspected.

d) *Learning problems*: Maternal and paternal learning problems were extracted from an intake form completed at the time of their FASD assessment. Information was reported as yes or suspected or suspected.

e) *Biological mother highest level of education*: Highest level of education completed was extracted from an intake form completed at the time of their FASD assessment. Information about biological father's highest level of education was not available.

f) *Sibling with FASD or PAE*: Sibling with FASD diagnosis or confirmed prenatal alcohol exposure seen by the clinic and relationship i.e. full or half sibling was extracted from a pediatrician clinical report conducted at the FASD assessment.

Prenatal factors

a) *Maternal age*: Age in years was extracted from a pediatrician clinical report conducted at the FASD assessment.

b) *Gestational age in weeks*: Birth term in weeks was extracted from a pediatrician clinical report conducted at the FASD assessment. Infants were considered premature if born before 37 weeks of gestation or full term if born on or after 37 weeks.

c) *Gestational weight*: Weight in grams was extracted from the pediatrician clinical report conducted at the FASD assessment. Low birth weight (LBW) was defined as less than 2500g.

d) *Head circumference*: Measurement of the child's head around the largest area at birth was extracted from a pediatrician clinical report conducted at the FASD assessment.

e) *Prematurity*: Premature birth was defined by gestational age less than 37 weeks or if infants were classified as premature in a pediatrician clinical report. Premature birth was confirmed based on a pediatrician clinical report conducted at the FASD assessment.

f) *Gravida*: Number of times a female has been pregnant, extracted from a pediatrician clinical report conducted at the FASD assessment.

g) *Parity*: Number of live births, extracted from a pediatrician clinical report conducted at the FASD assessment.

h) *Apgar score*: 1-minute and 5-minute Apgar scores (0-10) were extracted from a pediatrician clinical report conducted at the FASD assessment. A score of 7, 8, or 9 were considered normal, and a score of 6 or less were considered abnormal.

i) *Type of delivery*: Natural birth or ceasarean section was extracted from a pediatrician clinical report conducted at the FASD assessment.

j) *Birth complications*: yes or no birth complications was extracted from a pediatrician clinical report conducted at the FASD assessment.

k) *Emergency medical intervention*: Child received intensive care at birth was extracted from a pediatrician clinical report conducted at the FASD assessment.

l) *Perinatal complications*: Perinatal events included head injury, perinatal stroke, Jaundice, low heart rate, low iron, infection, seizures were extracted from a pediatrician clinical report conducted at the FASD assessment.

m) *Prenatal alcohol exposure*: prenatal alcohol exposure was confirmed prior FASD assessment based on birth records, maternal report, or a reliable source. Alcohol exposure was ranked using the 4-digit diagnostic system and Canadian guidelines at the time of the FASD assessment.

n) *Smoke*: prenatal smoke exposure was extracted from clinical file and/or a pediatrician clinical report conducted at the FASD assessment.

o) *Drug exposure*: prenatal exposure to drugs was extracted from a pediatrician clinical report conducted at the FASD assessment.

p) *Medication use during pregnancy*: prescribed medications were extracted from a pediatrician clinical report conducted at the FASD assessment.

q) *Maternal medical condition*: maternal medical condition during pregnancy (e.g. epilepsy, infection) was extracted from a pediatrician clinical report conducted at the FASD assessment

r) *Maternal stress*: Adverse life stressors during pregnancy such as domestic violence, transient lifestyle, were extracted from a pediatrician clinical report conducted at the FASD assessment.

s) *Maternal mental health*: maternal mental health issues during pregnancy were extracted from a pediatrician clinical report conducted at the FASD assessment.

Postnatal factors

a) Living situation or type of care: Child living with biological family, adoptive family, foster family, or other (e.g. group home) at the time of their FASD assessment, extracted from clinical file.

b) *Caregiver relationship status*: Child living in a single or two parent home, extracted from clinical file.

c) *Abuse*: Child ever experience physical, sexual, or emotional abuse, extracted from clinical file.

d) *Neglect*: Child ever experience not having basic needs met or emotional neglect, extracted from clinical file.

e) Abandonement: Child ever experience abandonement from a primary caregiver or biological parent, extracted from clinical file.

f) *Number of placements*: Total number of different living placements, extracted from clinical file.

g) *Multiple moves*: Total number of moves within one placement, extracted from clinical file.

h) *Time in placement*: Length of time in current living placement, extracted from clinical file.

i) *Domestic violence in home*: History of living in a home with domestic violence, extracted from clinical file.

j) *Drugs and alcohol in home*: History of living in a home with drugs and alcohol, extracted from clinical file.

k) *Trouble with the law*: History of living in a home with a parent with legal problems or incarceration, extracted from clinical file.

l) *Mental health*: History of living in a home with a caregiver with mental health issues.

m) *Failure to thrive*: weight or weight gain is lower than that of a same age peer, extracted from clinical file.

n) *Malnourishment*: nutritional needs in early childhood not met, as reported in FASD assessment.

o) *Lack of early stimulation*: parental stimulation was not apparent or present, as reported in FASD assessment.

p) *Developmental delay*: Developmental milestones not met, was extracted from the FASD assessment report.

q) *Developmental behavioral/emotional issues*: History of emotional and behavioral issues in early childhood was extracted from the FASD assessment report.

r) *Child sleep problems*: Reported sleep issues or sleep disorder was extracted from the FASD

assessment report.

s) Childhood head injury: Reported head injury that involved loss of consciousness or medical attention, was extracted from clinical file.

t) *Child school problems*: History of difficulties in school, was extracted from the clinical file.

u) *Significant life event*: Family child was living with experienced bereavment (family member death), parental health problem, divorce, or other traumatic life event, was extracted from the FASD assessment report.

Appendix C

ACE Scoring Sheet
Score 10

Abuse *Has the child ever been a victim of….*

Physical *If yes enter 1* _____

Sexual *If yes enter 1* _____

Emotional ***If yes enter 1*** _____

Neglect: *Has the child ever….*

Been a victim of neglect?

and/or

Lived in a household where their basic needs were not met? *If yes enter 1* _____

Been a victim or emotional neglect? ***If yes enter 1*** _____

Household Dysfunction

Not Raised by Both Biological Parents *If yes enter 1* _____

Has the child ever lived in foster care?

Has the child been raised by both biological parents?

*Where the parents **ever** separated or divorced?*

Has the child ever lived in a household where….

Substance Abuse *If yes enter 1* _____

Someone misused alcohol or had a drinking problem?

Legal Trouble *If yes enter 1* _____

Someone was in trouble with the law?

Mental Illness *If yes enter 1* _____

Someone had a serious mental illness?

Domestic Violence *If yes enter 1* _____

They were exposed to domestic violence?

Other not specified ***If yes enter 1*** _____

They were reported to have chaotic home life, instability not specified

Don't count in score

Total Score /10 _____

Appendix D

Participant Information Form

The following questions aim to collect basic information about your child and your family. Please answer all of the following questions as they best describe your child. Feel free to ask for clarification of any of the questions.

GENERAL INFORMATION

Child's name (First/Middle/Last): _____

Date of Birth (Day/Month/Year): _____

Gender (M/F):_____

Age (years/months):_____

Ethnicity:_____

Parent/Guardian:_____

Contact Telephone: (_____)_____

Address: _____

_____

Email:_____

Form completed by: _____

Would you be interested in being contacted in the near future about related research?

☐ yes ☐ no

Identify your relationship to child: _____

Child is currently residing with (please circle):

- Biological Family (please specify) _____
- Foster Family (please specify)_____
- Adoptive Family (please specify)_____
- Group Home (please specify)_____
- Other (please specify)_____

Any unexpected changes in personal circumstance:

_____

_____

_____

_____

For both caregivers please indicate:

1. Caregiver's type of employment: _____

   Highest Grade Completed: _____

2. Caregiver's type of employment: _____

   Highest Grade Completed: _____

MEDICAL HISTORY

Did your child receive a diagnosis of an FASD?

☐ yes ☐ no

Does your child have an existing mental health diagnosis?

☐ yes ☐ no

***If yes, please check all mental health diagnoses that apply to your child**:*

MENTAL HEALTH DISORDER	**Current (Y/N)**	**Age Diagnosed**	**Diagnosed by?**
Attention Deficit Hyperactivity (ADHD)	☐ yes ☐ no	_____	_____
Anxiety Disorder	☐ yes ☐ no	_____	_____
Depression	☐ yes ☐ no	_____	_____
Bipolar Mood Disorder	☐ yes ☐ no	_____	_____
Oppositional Defiant Disorder	☐ yes ☐ no	_____	_____
Conduct Disorder	☐ yes ☐ no	_____	_____
Substance Use Disorder	☐ yes ☐ no	_____	_____
Obsessive Compulsive Disorder	☐ yes ☐ no	_____	_____
Psychosis	☐ yes ☐ no	_____	_____

Schizophrenia ☐ yes ☐ no _____ _____

Trauma History ☐ yes ☐ no _____ _____

Attachment ☐ yes ☐ no _____ _____

Reactive Attachment Disorder ☐ yes ☐ no _____ _____

Other (please specify) _____

Is there a family history of mental health or psychiatric issues in the child biological family?

☐ yes ☐ no

Please specify the mental health disorder (s) including substance use, alcoholism etc. and their relationship to your child.

Mental Health Treatment

Is your child currently receiving mental health treatment or intervention?

☐ yes ☐ no

Please list all mental health treatment and/or intervention your child is currently receiving.

1. _____

Which healthcare professional(s) referred them to each of the above named service?

_____

2. _____

Which healthcare professional(s) referred them to each of the above named service?

_____

3. _____

Which healthcare professional(s) referred them to each of the above named service?

_____

4. _____

Which healthcare professional(s) referred them to each of the above named service?

_____

5. _____

Which healthcare professional(s) referred them to each of the above named service?

_____

Is your child currently taking any medication?

☐ yes ☐ no

Did your child take any medications before testing today?

☐ yes ☐ no **When was the last day/time:** _____

If yes, please circle all prescription medications that apply:

Medication	*Current*	*Age Started*	*Used to treat?*	*How effective?*
Ritalin	☐ yes ☐ no	_____	_____	_____
Dexedrine	☐ yes ☐ no	_____	_____	_____
Antidepressants	☐ yes ☐ no	_____	_____	_____
Cylert	☐ yes ☐ no	_____	_____	_____
Tranquilizers	☐ yes ☐ no	_____	_____	_____
Anticonvulsants	☐ yes ☐ no	_____	_____	_____
Antihistamines	☐ yes ☐ no	_____	_____	_____
Other (specify)	☐ yes ☐ no	_____	_____	_____

Thank you for your time and help with our study!