Psychosocial risk factors and health outcomes in the offspring of parents with bipolar disorder in adolescence and young adulthood: A 10-year longitudinal study

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ABSTRACT

Psychosocial risk factors and health outcomes in the offspring of parents with bipolar disorder in adolescence and young adulthood: A 10-year longitudinal study

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It is well known that the offspring of parents with bipolar disorder (OBD) are at heightened risk of developing mental disorders, particularly the affective disorders. However, we have much less information about deleterious non-psychiatric outcomes, such a health-risk behaviors, and the family-environmental risk factors associated with negative outcomes in the OBD. It has been proposed that the OBD, through genetic mechanisms and early family interactions, develop a heightened sensitivity to stress, maladaptive coping, and dysregulated behavior, which ultimately increases the risk for affective disorders. The current dissertation was designed to test parts of this model by conducting a comprehensive assessment of social risk factors, personality, and mental health in the OBD, and to examine putative antecedents of negative outcomes in the OBD using 10-year longitudinal data. The first study within this dissertation assessed different psychosocial and health-related outcomes in the OBD, including mental health, personality, coping style, smoking, suicidality, high-risk sexual behaviors, criminality, and mental health. These factors were compared across affected and unaffected offspring in order to differentiate potential prodromal markers from correlates of mood episodes. It was found that unaffected OBD engaged in less task-oriented and more avoidant coping strategies than controls. Furthermore, after controlling for current affective disorders, the OBD were more likely than controls to engage in sexual risk behaviors (SRBs). In the

second study, parents' personality, specifically high neuroticism, was assessed to determine whether it predicted SRBs among the offspring 10 years later, and whether the relationship between parents' personality and offspring SRBs was mediated by behavioral problems in middle childhood. High neuroticism, low agreeableness, and low extraversion in the parents predicted SRBs in their offspring in late adolescence-early adulthood. The offspring's externalizing problems in middle childhood partly mediated the association between parents' personality and offspring SRBs. The findings highlight a risk profile in the OBD characterized by poor stress coping and engagement in risky sexual behaviors. Furthermore, SRBs were related to a developmental trajectory that included markers of family stress and early externalizing problems. Together, these studies highlight the importance of behavior problems as markers of vulnerability in the OBD. Importantly, this pattern of results emphasizes the need for targeted, early interventions aimed at increasing familial stability and stress management before the development of behavioral problems.

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Rami Nijjar conducted the statistical analyses and wrote the first draft of the manuscript. Mark Ellenbogen, Sheilagh Hodgins, and Rami Nijjar edited subsequent versions of the manuscript. All authors contributed to and approved the final manuscript.

Study 2:

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1. INTRODUCTION

Understanding the development and progression of poor mental health is a central goal of health care research. One effective method of achieving this goal is through tracking the development of those who are at high familial risk of experiencing mental disorders. Prospective longitudinal studies provide us with the unique opportunity to identify traits and behaviors that may signify early markers of risk for psychopathology, as well as environmental factors that may exacerbate genetic vulnerability. Currently there exists an extensive literature on children of depressed parents that shows compromised functioning in biological, cognitive, behavioral and social domains (for review see Edwards, Castle, Mills, Davis, & Casey, 2014; Goodman & Tully, 2006). However, considerably less is known about the offspring of parents with bipolar disorder (OBD). There is large a body of evidence describing the prevalence of mental disorders in this population (i.e. Duffy, Horrocks, Doucette et al., 2014; Goldstein,. Shamseddeen, Axelson et al., 2010; Mesman, Nolen, Reichart et al., 2013; Vandeleur, Rothen, Gholam-Rezaee et al., 2012). One review of the literature of studies conducted before 1997 concluded that the OBD are 2.7 times more likely than the general population to develop BD and 4 times more likely to develop an affective disorder (LaPalme, Hodgins, & Larouche, 1997). A subsequent review by Delbello and Gellar (2001) concluded that the prevalence of psychiatric disorders in children and adolescent OBD ranged from 5-67%, compared to 0-38% in offspring of healthy parents. As would be expected, prevalence of psychopathology increases steadily as the OBD move through adolescence and young adulthood (i.e. Hillegers, Reichart, Wals et al., 2005). Overall, prospective studies estimate that by adolescence 40-50% of the OBD will have developed a mood disorder,

and 10-20% will have developed bipolar disorder (Duffy, Alda, Crawford et al., 2007; Hillegers et al., 2005). Little is known, however, about either non-psychiatric risk factors or the progression of prodromal symptoms into adolescence and young adulthood within this population. Furthermore, the specific factors that constitute familial environmental risk remain elusive. As mechanisms of risk are complex, developmental perspectives that consider transactional processes are required to understand chains of causation (Hinshaw, 2004).

This set of studies sought to address the paucity of literature by, (1) conducting a comprehensive examination of psychosocial risk factors, including personality, stress coping, and problem behavior, in the OBD; (2) examining the continuity of behavioral problems in the OBD as they enter adolescence and young adulthood; and (3) assessing how the personality of parents may perpetuate risk trajectories. These studies were situated in a broader literature of pathological development in the OBD and served to elucidate risk pathways and opportunities for prevention. This introductory chapter proposed to highlight gains in the quantitative literature on the OBD and present the rationale of the subsequent studies. The text below offers insight into factors implicated in the development of affective disorders in general and BD in particular. This includes a discussion of the environmental factors specific to BD families that may perpetuate risk. I then outlined what is currently known about psychosocial functioning in the OBD so as to create a foundation for the rationale of this dissertation.

1.1 The Development of BD

BD is associated with the highest heritability estimate of all psychiatric illnesses including schizophrenia (Smoller & Finn, 2003; Farmer, Elkin, & McGuffin, 2007). As

stated by Merikangas and Low (2004), "a positive family history is the most potent risk factor for mood disorders, particularly bipolar disorder." Evidence for this is shown in family studies of first- and second-degree relatives of bipolar probands. These studies estimate a 10-fold increased risk of BD in family members when compared to population base rates and controls (Smoller & Finn, 2003). Having a relative with BD appears to increase the risk of developing both BD and unipolar depression (McGuffin, Katz, & Eldrich, 1986). However, those with a relative with unipolar depression have not been found to be at greater risk of developing BD than the normal population (Gershon, Hamovit, Guroff et al., 1982; Weissman, Gershon, Kidd et al., 1984). Interestingly, even though BD is highly heritable, there is some suggestion that having a parent with BD is associated with lower risk of developing psychopathology than having a parent with depression (e.g. Hammen, Burge, Burney et al., 1990).

In general, the mechanisms of risk associated with maladaptive development are complicated and multifaceted. For instance, parents transmit both genes and shared environmental influences (i.e. family environment). As such, family studies provide no conclusive evidence of the genetic basis of the disorder. By comparing twin pairs matched for shared environment but differing in degree of genetic relatedness, twin studies provide a more clear understanding of the genetic contribution of BD. Four such methodologically rigorous studies evidenced concordance rates of 5-19% in dizygotic twins and 36-67% in monozygotic twins, with heritability estimates ranging from 59–87% (Bertelsen, Harvald, & Hauge, 1977; Cardno, Marshall, Cold et al., 1999; Kendler, Pedersen, Johnson, Neale, & Mathe, 1993; McGuffin, Rijsdijk, Andrew et al., 2003), providing support for a robust genetic contribution in the development of BD.

1.1.1 Gene-environment interactions

The strong heritability factor of BD has prompted numerous molecular genetic studies aimed at identifying specific genes associated with the disorder. However, decades of inconclusive linkage and gene association studies have encouraged a shift towards an exploration of gene-environment interactions (see Etain, Henry, Bellivier, et al., 2008; McGowan & Kato, 2007; Rutter, 2010). The underlying assumption is that while both genetic and environmental factors contribute to the disorder, these components interact synergistically, with genes influencing the environment that one selects as well as their susceptibility to stressful environments (Caspi & Moffitt, 2006; Rutter, 2010). Across the life-span several environmental factors have been identified as contributors to risk of developing BD and other mood disorders. These factors include, but are not limited to, season of birth, inadequate prenatal nutrition, prenatal stress, pre-term birth, obstetric complications, childhood maltreatment and social disadvantage, substance use during adolescence, and stressful life events (see Uher, 2014). However, a growing body of empirical literature supports that genes moderate the contribution of environmental factors to the development of mood disorders. For example, research shows that a polymorphism on the serotonin transporter gene promoter region (5-HTTLPR) moderates the effects of stressful life events on the risk for development of major depressive disorder (Caspi, Sugden, Moffitt et al., 2002; Brown, 2012). Similarly studies have documented the moderating effect of the brain-derived neurotrophic factor Met allele on the contribution of both childhood maltreatment (Miller, Hallmayer, Wang et al., 2013) and stressful life events (Hosang, Uher, Keers, et al., 2010) to the chronicity and severity of mood episodes in BD patients. In addition, the paranoxonase 1 (a

hydrolytic antioxidant enzyme) QQ genotype has been shown to moderate the impact of smoking behavior on the risk for developing BD and major depression (Bortolasci, Vargas, Souza-Nougeuira, et al., 2014). Given the observed interplay between genetic and environmental factors on the development of mood disorders, a greater understanding of potential endophenotypes (i.e. behavioral and cognitive risk markers) would contribute well to our understanding of adaptive and maladaptive development in the OBD. Elucidating risk markers would allow us to better understand stress susceptibility and psychopathological progression in this population.

1.1.2 The role of stress

The relationship between stress and the development of affective disorders, in general, is well-established (Kessler, 1997; Hamman, 2005). Given evidence of overlap between the genetic liability to develop depression and the genetic liability to experience stressful life events (Kendler & Karkowski-Shuman, 1997; Kendler, Karkowski, & Prescott, 1999; Farmer et al., 2007), it has been suggested that life stress is integral to the development of affective disorders (see Paykel, 2001 for review). For example, stressful life events (SLEs) have been shown to precede the onset and relapse of mood episodes (e.g., Kendler, et al.,1999). SLEs have been defined as "circumstances punctually situated in time that induce stress and require the individual to use adaptation mechanisms" (Ezquiaga, Ayuso Gutierrez, & Garcia Lopez, 1987; p. 136); these are stressors that are acute and time-limited. Hillegers et al. (2004) measured SLEs retrospectively in a sample of adolescent OBD and found that stress levels were associated with a 10% increase in the risk of disorder onset. Additionally, Horesh and Iancu (2010) found that both individuals with depression and those with BD reported more stress in the year preceding

their first episode compared to control participants. Using a prospective design, Hunt, Bruce-Jones, and Silverstone (1992) demonstrated an almost 4-fold increase in negative life events prior to relapse in patients with bipolar spectrum disorders. As such, it would appear that life stress plays a key role in the development of psychopathology.

Chronic life stress defined as, "adverse circumstances that act uninterruptedly over a prolonged time" (Ezquiaga et al., 1987; p. 136), is another vulnerability factor in the development of affective disorders. Brown and Harris (1978) were the first to show that chronic stress was associated with the onset of depression in women. Similarly, individuals diagnosed with depression were seven times more likely to report having experienced a chronic stress prior to the onset of depression compared to non- affected controls (Rojo-Moreno, Livianos-Aldana, Cervera-Martinez, Carabantes, & Reig-Cebrian, 2002). Furthermore, McGonagle and Kessler (1990) found chronic stress to be a better predictor of sub-clinical depressive symptoms than SLEs, further supporting an important environmental component in the development of mood disturbances. Similarly, both life stress (Tsuchiya, Byrne, & Mortensen, 2003), and family environments that are high in conflict and emotional over-involvement (i.e. Kim & Miklowitz, 2004; Miklowitz, Axelson, George et al., 2009; Miklowitz, Goldstein, & Nuechterlein, 1995; Miklowitz, Goldstein, Nuechterlein, Synder, & Doane, 1987, Miklowitz, Velligan, Goldstein et al., 1991) have been implicated in the clinical course, chronicity, and treatment outcomes for BD. In a sample of adolescent OBD diagnosed with BD, chronic stress in the family and in romantic relationships predicted less improvement in depressive and manic symptoms following treatment (Kim, Miklowitz, Biuckians, & Mullen, 2007). In our studies, we have found evidence that, independent of affective disorder diagnosis, parents with BD

experienced more interpersonal and non-interpersonal chronic stress, as compared to control parents (Ostiguy, Ellenbogen, Linnen et al. 2009). This would suggest that families with BD parents are situated within conflictual family and social environments, increasing stress and diminishing social support. Taken together, it would seem that life stress not only impacts symptomatic development in the OBD, but also exacerbates symptoms in BD parents, contributing to compromised family functioning.

The stress generation theory, proposed by Constance Hammen (1991) suggests an important bidirectional association between stress and depression. Dependent life events, which are defined as life events that are due to the behaviors or characteristics of the person (Hammen, 1991), have been proposed to be particularly relevant to the development of depression. This theory is largely based on findings that depressed women reported more dependent SLEs than women with BD, women with a chronic physical illness, or healthy controls (Hammen, 1991). Depressed women also reported more SLEs of an interpersonal nature than all the other groups. From this, Hammen concluded that depressed individuals are more likely than non-depressed individuals to create stressors that are interpersonal and, in part, dependent on their own behaviors. There is varied support for stress generation in BD patients, with some studies finding no evidence for this (Grandin, Alloy, & Abramson, 2007; Hammen, 1991; Reilly-Harrington, Alloy, Fresco, & Whitehouse, 1999). However, one study showed that participants with BD who were in a depressive episode did not generate more negative, dependent SLEs, but experienced fewer positive interpersonal events than controls (Bender, Alloy, Sylvia, Urosevic, & Abramson, 2010). Furthermore, participants in a hypomanic episode experienced more dependent positive and negative interpersonal events than controls.

Recently, Molz and colleagues (2013) have shown that trait levels of hostility and impulsivity predicted levels of dependent and independent life events in individuals with bipolar spectrum disorders, supporting the premise that characteristics of the person contribute to the experience of stress in this population. Similarly, another study examining parents with BD and parents with no mental disorders who were divided on high versus low trait neuroticism (Ellenbogen & Hodgins, 2004) showed that individuals with BD who also displayed high neuroticism reported more dependent stressors than individuals with BD who displayed low neuroticism. In study of life stress in the OBD (Ostiguy et al., 2009), the OBD did not report more dependent life events compared to a group of control offspring, but they did experience more severe independent life events when compared to the control group. Taken together, these findings suggest that the OBD do not generate stress in their lives but rather are exposed to stress that may in part be due to living with an affectively-ill parent (see Ostiguy et al., 2012). Furthermore, there appears to be an important, yet understudied link between personality traits displayed by the affected parents and interpersonal stress within the family environment.

1.1.3. The Role of the Family Environment

The family environment represents an important means by which emotional and behavioral problems are perpetuated and maintained in offspring. Hostile parenting behavior, for example, has been suggested as one way in which aggressive behavior is conferred across the generations (Brooks, Whiteman, & Zheng, 2002; Conger, Neppl, Kim et al., 2003; Thornberry, Freeman-Gallant, Lizotte et al., 2003). Essentially, the early family environment provides social experiences that shape the behavior of the offspring, setting the foundation for self-regulation later on (Basic Behavioral Science

Task Force of the National Advisory Mental Health Council, 2006). As individuals with BD become parents, features of the disorder, and the consequences of these features on the family environment, may interact with genetic factors to put offspring at risk for maladaptive development. For example, as will be described in greater detail below, BD in parents may contribute to stressful, unstructured household environments, inconsistent parenting practices, and low-income status (Ellenbogen & Hodgins, 2004; McPherson, Dore, Loan, & Romans, 1992). These factors increase environmental stress and parents may also model ineffective coping for offspring. As such, genetic liability passed on from parent to offspring may be exacerbated (or activated) by environmental factors associated with having a parent with BD.

1.1.3.1 Family environment in BD families

Given the suggested implications of family environment on development of the OBD, a number of studies have sought to examine family environmental variables that may distinguish families with BD from unaffected families. In general, families environment in which a parent has BD have been characterized as stressful, chaotic, unpredictable, and may fail to teach children appropriate skills for coping with stress (Chang, Blasey, Ketter, & Steiner, 2001; Ellenbogen & Hodgins, 2004). This has been exemplified by several studies of BD families. For example, Chang and colleagues (2001) collected parental ratings from 36 BD families (56 children) on the Family Environment Scale. When compared to published norms, BD families reported lower cohesion and organization and more conflict. These results did not differ across families with two mood disordered parents compared to those with only one parent with BD. Similar results have been found in controlled studies conducted in the U.S.(Romero,

Delbello, Soutullo et al., 2005), Brazil (Ferreira, Moreira, Kleinman et al., 2013) and the UK (Barron, Sharma, Le Couteur et al., 2014). Furthermore, lower cohesiveness and organization, less encouragement of the expression of feelings, and higher conflict was found in families with BD versus controls even after controlling for group differences in socioeconomic status (Romero et al., 2005; Barron et al, 2014). Ferreira et al. (2013) also found that the presence of psychiatric disorders in the OBD was associated with higher levels of parental control. Lower cohesion and expressiveness and more conflict were also reported in parents of BD children compared to families with no BD offspring (Belardinelli, Hatch, Olvera et al., 2008). Taken together, results from investigations of families with BD present suggest that family members have greater difficulty with co-operation and structure than the average family. This may be one factor that leads to heightened stress in the lives of family members.

1.1.3.2 Parent-child interactions

A cardinal feature of BD that exists across mood episodes is marked irritability or general inability to regulate negative emotion (Hanwella & de Silva, 2011); this is likely to have a negative impact on the way in which individuals with BD interact with others, including close family members. Indeed, research on families of individuals with BD reveals signs of problematic family interactions. For example, a study comparing families of BD patients to families of schizophrenic patients showed that parents of BD patients used more criticism, had a more negative affective style, and used poorer coping during conflict interactions (Miklowitz et al., 1995). Moreover, high levels of expressed emotion within the family (i.e. critical comments, emotional over-involvement or hostility) appear to be positively related to relapse rates in BD patients (Butzlaff & Hooley, 1998),

highlighting the impact of family environment on mental health. Furthermore, high levels of chaos within the family environment have been linked to parents' over-reactivity (Calam, Jones, Sanders, Dempsey, & Sadhnani, 2012), suggesting that lack of structure within the family environment may exacerbate negative interactions amongst family members. Overall communication may also be compromised in these families. For example, Miklowitz and colleagues (1991) identified an ineffective communication style in BD patients when they interacted with family members. This style of communication was characterized by difficulties in sharing a focus of attention with their conversation partner, communicating a message clearly, or bringing about closure when discussing ideas.

There is evidence that both parents with BD and their children contribute to negative family interactions. On the part of the parent it has been shown that parents with BD exhibit lower levels of expressiveness and more negative communication styles when interacting with their children than controls (Vance, Huntley, Jones, Espie, Bentall & Tai, 2008), with some support that mothers with BD react more negatively towards their children than mothers with major depression (Inoff-Germain, Nottelmann & Radke-Yarrow, 1992). Mothers with BD have also exhibited a lack of boundaries and intrusive parenting styles, and have shown more critical/irritable interactions with their preadolescent children than mothers with no psychiatric condition (Tarullo, DeMulder, Martinez et al., 1994). With respect to the OBD, it would appear that, as early as age two, they show increased aggressiveness in interactions with their parents and exhibit over-concern about their parents' emotional discomfort (Zahn-Waxler, McKnew, Cummings, Davenport & Radke-Yarrow, 1984). There is also evidence that the OBD report more

insecure attachment to parents than controls (Radke-Yarrow et al., 1985; Zahn-Waxler et al., 1984), further suggesting that parent-child interactions are compromised in this population.

Taken together, parents with BD and their children are prone to negative emotional reactivity and ineffective communication, which may be exacerbated by lack of structure within the household. These negative interactions may be one way in which risk could be conferred onto offspring. Evidence for this has been seen in the contribution of parents' emotional reactivity and household chaos to emotional difficulties in the OBD (Calam et al., 2012). Early measures of maternal negativity have also shown association with impairment on tests of executive functions, which are integral to emotion regulation (Meyer, Carlson, Wiggs et al., 2006). As such, it is likely that negative family interactions are important environmental risk factors for the OBD that warrant further attention.

1.1.3.3.Neuroticism in parents

Parental personality traits impact parenting practices. First proposed by Belsky (1984), this claim has since received substantial empirical support (see Prinzie, Stams, Dekovic, Reijnjtes, & Belsky, 2009). In particular, high trait neuroticism (a trait reflecting high levels of negative emotionality and emotional reactivity) and low agreeableness (a trait reflecting high levels of antagonism and low empathy; Costa & McRae, 1992) are uniquely related to harsh, coercive parenting (e.g. Bugental & Shennum, 1984; Prinzie et al., 2009). Parents high in neuroticism have been shown to exhibit less warmth, sensitivity and responsiveness, and more intrusiveness, power assertion and hostility than those low in neuroticism (Belsky, Crnic, & Woodworth,

1995; Bornstein, Hahn, & Hayes, 2011; Clark, Kochanska, & Ready, 2000; Kochanska, Askan, & Nichols, 2003; Kochanska, Clark, & Goldman, 1997). Neuroticism has also been associated with a wide range of parents' behaviors, such as interpersonal conflict, maladaptive parenting, and ineffective coping (Ellenbogen & Hodgins, 2004; Oppenheimer, Hankin, Jenness, Young, & Smolen, 2013; Prinzie et al., 2009). Furthermore, it would appear that high parental neuroticism and low agreeableness are associated with behavioral problems and insecure attachment in children (Kochanska et al., 1997) and antisocial behaviors and adjustment problems in adolescence (Conger, Conger, Elder, & Lorenz, 1992; Nigg & Hinshaw, 1998; Van Os & Jones, 1999). These, studies would suggest that parents' personalities not only impacts parenting and parent behavior, but also predict problematic outcomes in offspring across development.

One model of intergenerational risk transmission postulates that offspring whose parents display high trait neuroticism not only inherit the tendency to overreact to daily hassles, but also are privy to having ineffective coping skills modeled to them by their parents, as well as to the use of poor parenting practices (Ellenbogen & Hodgins, 2004). As such, it is suggested that parents' neuroticism confers risk to offspring indirectly by creating stressful, chaotic, and unstable family environments, and by using parenting practices that fail to protect children from stress. In support of this model, high levels of neuroticism in parents have been shown to be associated with low psychosocial functioning, poor parenting, ineffective coping and more dependent SLEs in parents (Ellenbogen & Hodgins, 2004) and more emotional and behavioral problems in offspring (e.g. Kochanska, Clark, & Goldman, 1997; Ostiguy et al., 2012; Rubin, Hastings, Chen et al., 1998). More recently, it was found that parents' neuroticism predicted concurrent

childhood internalizing and externalizing behavior problems, with this association being stronger in the OBD than in control families (Ostiguy, Ellenbogen, & Hodgins, 2011). In this study parents' neuroticism was also associated with deficits in offspring interpersonal functioning 10 years later and that this association was mediated by childhood internalizing behavior problems (Ostiguy et al., 2011). This suggested that having a parent with both BD and high neuroticism could negatively impact offspring outcomes early in childhood as well as later on in development. However, further studies of the OBD and their parents are necessary to clarify this proposed association.

1.1.4 Summary

Research on the genetic, environmental and familial risk factors associated with OBD risk status would suggest that there are complex and multiple pathways to maladaptive development in this population. In particular, it would appear that life stress - including the stress related to disorganized family environments and maladaptive communication patterns among family members - contribute to vulnerability in this population. Studies of the OBD indeed suggest that this group displays compromised emotional and behavioral functioning compared to their peers. However, much of what is known of the OBD centers on psychiatric outcomes. Given the interplay between genetic effects and environmental moderators for complex mental disorders (see Cicchetti, 2007; Rutter, Dunn, Plomin et al., 1997; Rutter, 2009), it is important to study psychosocial risk factors, and the contribution of specific parental traits, in parallel with mental health outcomes in the OBD, in order to develop more comprehensive etiological models of affective disorders. Knowledge of such factors would contribute to the creation of well-timed, targeted preventative interventions for the OBD.

1.2 Risk factors in the offspring of parents with bipolar disorders

In addition to mental disorders, the OBD are also likely at risk for a range of psychosocial outcomes that impact functioning years before the development of pathological symptoms. Signs of maladaptive development, including negative affect, ineffective coping, behavior problems, and difficulty in interpersonal interactions, may signify a general difficulty in socio-emotional regulation that contributes to significant dysfunction in this population. The following is a summary of research on risk factors in the OBD to date.

1.2.1 Behavior Problems

The OBD children appear at heightened risk of developing both internalizing (depressive, anxious, and/or somatic symptoms) and externalizing (aggressive behavior and rule-breaking/delinquency) behavior problems during childhood (i.e. Klimes-Dougan, Long, Lee et al., 2010; Ellenbogen et al., 2006; Zahn-Waxler, et al., 1984). The OBD may develop internalizing and externalizing problems later on in childhood, albeit at a slightly lower rate than the children of depressed parents (Andersen & Hammen, 1993; Hammen, Burge, Burney, & Adrian, 1990; Radke-Yarrow, Nottelman, Martinez, Fox, & Belmont, 1992). However, there is suggestion that externalizing behaviors are particularly salient in this population (see Hodgins, Faucher, Zarc, & Ellenbogen, 2002)

Externalizing behavior problems are defined by high novelty seeking, behavioral disinhibition, and problems regulating anger (e.g. Oldehinkle, Hartman, De Winter et al., 2004; Radke-Yarrow et al., 1992; Rothbart, Ahadi, & Evans, 2000; Shiner & Caspi, 2003). These traits have been evidenced in the OBD from an early age (Hirschfield-

Becker, Beiderman, Calltharp, Rosenbaum, Faraone, & Rosenbaum, 2003; Hirschfield-Becker, Beiderman, Henin, et al., 2006). Importantly, problems that are encompassed by externalizing patterns, including disruptive behaviors and attentional difficulties, are thought to confer risk of psychological problems in the OBD later on (i.e. Calam, Jones, Sanders et al., 2012; Calkin & Howse, 2004; Duffy, 2012; Meyer, Carlson, Wiggs, et al., 2004; Dienes, Chang, Blasey, Adleman, & Steiner, 2002; Giles, Delbello, Stanford & Strakowski, 2007). For example, in their longitudinal comparison of OBD with the offspring of parents with other forms of psychopathology, Carlson and Weintraub (1993) found that, although elevated behavioral and attentional problems were seen across all risk groups, the relationship between these childhood problems and the development of affective disorders in young adulthood was specific to the OBD (Carlson & Weintraub, 1993). These results have since been replicated (i.e. Egeland, Shaw, Endicott et al., 2003). Moreover, there is evidence that childhood externalizing problems may contribute to difficulties with reality testing later in life (Klimes-Dougan et al., 2010), further highlighting externalizing behavior problems as an early marker of risk.

Although overall the literature would suggest that the OBD are more apt to display childhood behavior problems, the stability of such problems across development is not known. There is some suggestion of continuity of internalizing problems. For example, childhood anxiety is suggested to be an important early marker of risk for mood disorders later on in the OBD (Duffy, Horrocks, Doucette et al., 2013). The known trajectories of childhood externalizing problems in high-risk populations likewise remain elusive. Childhood externalizing problems are thought to represent early signs of self-regulatory deficits (Calkins & Howse 2004). One way in which externalizing problems

may cause problems later on is that " ongoing disturbances in self-regulation accumulate over time, resulting in disruption to core internal regulatory processes including reality testing (thought problems) and internalized feelings of distress" (internalizing problems; Klimes-Dougan, Long, Lee, et al., 2010, pp.849). In the general population, externalizing behaviors seem to show a normative decrease across childhood, (i.e. Gilliom & Shaw, 2004; Mathieson, Sanson, Stoolmiller, & Karevold, 2009). However, results from a recent large-scale study of Dutch adolescents suggest that while aggression and anxious/depressed behavior decrease, rule-breaking behavior increases across adolescence for both boys and girls, (Ormel, Oldenhinkel, Sijtsema et al., 2012).

Unfortunately, the stability of behavior problems across development in the OBD is not known. It is suspected that persistent impulsive and anti-social behaviors represent a distinct pattern of inherited vulnerability (Kovacs et al., 1997; Williamson et al., 1995). A key distinction has been made between " life-course persistent" and "adolescent limited" problem behavior (Moffitt, 1993). The former is thought to be partly heritable and linked to emotional, behavioral, and occupational difficulties across the lifespan. These behavioral patterns are thought to reflect heterotypic continuity, where the continuity of a trait or attribute is assumed to underlie diverse, but conceptually similar, phenotypic behaviors (Kagan, 1969; Rutter, Kim-Cohen, & Maughan, 2006). It is further suggested that life course persistent behaviors are influenced by disrupted parent-child relationships in which parents have difficulties coping with a difficult child (Moffitt, 1993). Adolescent limited problem behavior encompasses normative "acting out " behaviors that are seen in adolescents as they attempt to assert their autonomy. This pattern of problem behavior, is, as the name suggested, time-limited and not thought to be

indicative of a maladaptive trajectory. As the OBD are prone to behavior problems in childhood, understanding the continuity of such behaviors as they develop may be integral to the search for relevant endophenotypes in this population. Furthermore the studying of adolescent behavior may be particularly relevant to understanding processes by which the OBD contribute to their own risk for maladaptive development. As individuals enter adolescence they begin to self-select environments that may further exacerbate dispositional traits and create stress for themselves. Caspi, Elder, and Bem (1987, 1988, 1989) provide two compelling explanations as to how this may occur. First, individuals seek out environments that sustain their personality dispositions. Second, the behavior of an individual selects them into an environment that promotes further maladaptive behavior. For example, aggressive behavior may lead to dropping out of school, which may in term influence the selection of peer groups, leading to more anti-social/aggressive behavior. As is also important to note, females may manifest aggressive tendencies through relational and sexual means that are less explicit (Radke-Yarrow, Nottelman, Martinez et al., 1992; Serbin & Karp, 2004), warranting the study of a broad range of deviant or "acting out" behavior.

1.2.2 Stress Sensitivity

Biological sensitivity to environmental stressors may be one important risk factor differentiating the OBD from controls. An early study of the OBD showed that the OBD exhibited heightened physiological responses to stress and also had significant correlation between autonomic nervous system activity and anxiety during both rest and arousal phases (Zahn, Nurnberger, Berrettini, & Robinson, 1991). This pattern of results was not found in the control population. OBD have also been shown to exhibit abnormal

hypothalamus-pituitary-adrenal (HPA) axis functioning, as indexed by heightened diurnal salivary cortisol levels (Ellenbogen, et al., 2006; Ellenbogen et al., 2010). These results were found to be independent of psychopathology in the offspring. This may be especially important given that prospective studies of the OBD (Ellenbogen et al., 2011), as well as youth deemed to be high risk by virtue of having a mentally ill parent or having been exposed to psychosocial adversity (Goodyear et al., 2009), have demonstrated that high diurnal levels of salivary cortisol predict the development of affective disorders in subsequent years. More recently, it was shown that OBD experiencing high levels of interpersonal stress showed higher daytime cortisol levels than OBD experiencing low levels of interpersonal stress. This interaction was not seen in control offspring, demonstrating that the OBD are more biologically sensitive to interpersonal stress than offspring of parents with no mental illness (Ostiguy, Ellenbogen, Walker, et al., 2011). As such, the OBD may be vulnerable to affective disorders, in part, by virtue of biological stress sensitivity.

1.2.3 Cognitive style

There is evidence that the OBD engage in maladaptive cognitive styles. One of the earliest studies to examine cognitive factors in the OBD found that the high-risk offspring were more likely to endorse a less positive self-concept and a more negative attributional style compared to the offspring of medically ill or control mothers (Jaenicke et al., 1987). However, early studies did not control for diagnoses, making it difficult to ascertain if the results are due to the risk status or to the presence of affective disorders in the OBD. Pellegrini and colleagues (1986) found that compared to unaffected OBD and controls, affected OBD showed deficits in social problem solving, self-esteem, and self-

perceived competence. Jones and colleagues (2006) assessed 25 adolescent OBD and 22 age- and sex-matched healthy controls. The authors found that the OBD showed more rumination, greater instability of self-esteem, and greater negative affect than healthy controls. Furthermore, affected OBD showed higher levels than unaffected OBD, though both OBD groups were elevated on these traits relative to controls. This finding was replicated in a subsequent study, despite a smaller sample size (Espie, Jones, Vance, & Tai, 2012). Furthermore, affected OBD were found to be less flexible and less task-oriented than their non-affected counterparts (Singh, DelBello, & Strakowski, 2008). A recent study showed that unaffected young adult OBD were more likely to endorse grandiose beliefs of one's own ideas and pursuit of goals (Ruggero, Bain, Smith & Kilmer, 2013). They were also more likely to endorse a cognitive style that suggested that one's autonomy must be asserted, even in the face of criticism from others. This was found even in those who had not yet developed a mood disorder. Similarly, in their review of the OBD literature, Narayan and colleagues (2013) suggest that OBD show disturbances in reality testing. Dysfunctional attitudes are important to consider within this population, as they may serve to exacerbate mood states and thereby heighten the risk of affective episodes (Thomas, Knowles, Bentall, & Tai, 2009).

1.2.4 Social competence

Lack of social competence may be an important risk marker in the OBD. For example, affected OBD have been found to have fewer close supportive relationships, poorer self-concept, and weaker support networks than their unaffected sibling (Pellegrini, Kosisky, Nackman et al., 1986). However, the overall level of social competence displayed by the OBD remains unclear. One study showed BD parents to

report low levels of prosocial behavior and high levels of problems with peers in their children (Calam, Jones, Sanders et al., 2012), however this study did not include a control group. Overall the evidence on social functioning in the OBD is mixed. Some studies have found better social functioning in the OBD when compared to control groups (Klein, Depue, & Krauss, 1986; Reichart, van Ende, Wals et al., 2007), while others show no significant impairment (i.e. Linnen, aan hot Ret, Ellenbogen et al., 2009; Reichart et al., 2004). In a naturalistic study, we tracked the social behaviors of young adult OBD and controls across a two-week period (Linnen et al., 2009). Although we found no overall group differences in interpersonal functioning, there were sex-specific differences showing that high-risk males displayed more quarrelsome and less agreeable behavior high-risk females. More recently we found that heightened quarrelsome behavior during social interactions was related to altered HPA activity in the OBD compared to controls (Ellenbogen, Linnen, Santo, aan het Rot, Hodgins, & Young, 2013). This would suggest that behavioral dysregulation during interpersonal interactions is interconnected with biological stress systems in the OBD.

1.2.5 Information processing and neuroimaging studies

The literature on OBD suggests that they may process social cues and emotional information in a discrepant manner. For example, one study showed that the OBD had greater difficulty correctly identifying facial emotions than members of the control group (Brotman, Guyer, Lawson et al., 2008). Furthermore, when presented with computerized displays of gradients of different facial emotions, the OBD required more intense emotional information to correctly identify and label a facial emotion than controls (Brotman, Skup, Rich et al., 2008). Finally, healthy OBD were shown to exhibit

attentional biases towards social threat and manic-irritable words, and showed better recall of negative words than children of healthy parents (Gotlib, Traill, Montoya, Joorman, & Chang, 2005). Neuroimaging studies provide support for information processing deficits in the OBD, although the results are somewhat mixed. For example, in one study, the OBD and the offspring of healthy parents performed a facial emotion-labeling task during fMRI (Mourao-Miranda, Oliveira, Ladouceur et al., 2012). Results showed that patterns of brain activation in the ventromedial prefrontal cortex during a task examining neural activity to happy versus neutral faces accurately discriminated between OBD and controls. The authors suggested that the OBD interpret neutral faces in the context of happy faces as ambiguous or even threatening. In this study the OBD did not differ from controls in accuracy of labeling facial emotions; all offspring had difficulty correctly labeling emotions (Mourao-Miranda et al., 2012). Another controlled neuroimaging study showed hyperactivation of the amygdala (an area of the brain implicated in threat processing) in the OBD while viewing both happy and fearful faces (Olsavsky, Brotman, Rutenberg et al., 2012). Similarly, amygdala hyperactivation has been shown in response to intensely happy faces in adult first-degree relatives of patients with BD (Surguladze, Marshall, Schulze et al., 2010). Ladouceur, Diwadkar, White, Bass, Birmaher, Axelson et al. (2013) found that unaffected OBD showed alterations in fronto-limbic system activity, an area implicated in voluntary emotional regulation, when compared to age-matched healthy controls. Specifically, unaffected OBD showed greater ventrolateral prefrontal cortex (VLPFC) activation in reaction of positive emotional stimuli and reduced VLPFC regulation of the amygdala in response to both positive and negative emotional stimuli. Neuroanatomical studies show the OBD to have greater

caudate nucleus volumes relative to controls (Hajek, Gunde, Slaney et al., 2009) as well as grey matter abnormalities in the inferior frontal gyrus, left anterior thalamus, left parahippocampal gyrus, and left hippocampus (see Nery, Monkul, & Lafer, 2013). Although it is difficult to interpret such a range of findings, results from these studies provide some evidence that the OBD differ from controls in brain structure and function. With regards to emotional information processing, despite heterogeneous findings, in part due to the use of a wide range of methodology, it would appear that the OBD interpret and/or react to socio-emotional cues in a manner that is distinct.

1.2.6 Executive functioning, school performance, and IQ

Meyer and colleagues (2004) found adolescent OBD who went on to develop BD in adulthood showed greater impairment in tests of executive function compared to controls. More recently, using a battery of neuropsychological tests, Klimes-Dougan, Ronsaville, Wiggs, and Martinez (2006), found that, when compared to offspring of depressed mothers and controls, OBD evidenced more problems with executive functioning, spatial memory, and sustained attention. These findings have since been replicated (Mazaide et al., 2009). In addition, unaffected siblings of children with pediatric BD show greater impairment on tasks of working memory and abstract problem solving compared to controls (Doyle, Wozniak, Wilens et al., 2009). Deficits in executive function may put the OBD at risk for poor emotional regulation and overall functioning. Furthermore, child and adolescent OBD exhibit significantly higher verbal than performance IQ (Decina, Kestenbaum, Farber et al., 1983; Kron, Decina, Kestenbaum, Farber, Gargan, & Fieve, 1982; Kestenbaum, 1979) and there is evidence of lower global IQ scores in the OBD versus controls (Maziade et al., 2009). During the school years, the OBD are more likely

to be put in special classes, display anti-social behavior in school, and have poor academic performance (Henin et al., 2005; McDonough-Ryan et al., 2002). Furthermore, McDonough-Ryan and colleagues (2002) found that 39% of the OBD who had academic problems showed significant Verbal-Performance IQ discrepancies. Taken together, deficits in information processing, executive functions, and intellectual functioning may contribute to risk profiles in the OBD, rendering them vulnerable to poor social and academic performance.

1.2.7 Personality

To date, we possess a limited understanding of the personality structure of the OBD. Personality traits may be partly heritable (Eaves, Heath, Martin et al., 1999; Plomin, DeFries, McClearn & McGuffin 2001; Benjamin, Ebstein, & Bellmaker, 2002) and are also influenced by non-genetic familial factors (Rutter, Dunn, Plomin et al., 1997). There is extensive literature linking personality traits, such as neuroticism (i.e. emotional instability and mood lability) to depression (Clark, Watson, & Mineka, 1994; Sass & Junemann, 2003; Christensen & Kessing, 2006). However, much less is known about the link between personality and BD. Moreover, there is ongoing debate as to whether personality is a cause or an effect of mood episodes (see Klein, Durbin, Shankman, & Santiago, 2002). Studies of OBD populations evidence abnormal trait-like behaviors from an early age. For example, a small scale study of OBD aged 15-18 months showed that they displayed more negative affect than offspring of healthy mothers and were slower to recover once upset (Gaensbauer, Harmon, Cytryn et al., 1984). From pre-school age, the OBD show higher levels of affective expressiveness (Kron et al., 1982; Decina, 1983), and are more active than their peers (Kron et al., 1982;

Decina, 1983; Chang, Blasey, Ketter, & Steiner, 2003). As adolescent and young adults, the OBD show a clustering of personality traits characterized by depressive reactivity, and emotional instability (Grigoriou-Serbanescu, Christdorescu, Totoescu et al., 1991). Several studies have also suggested that irritability and mood liability are particularly salient prodromal markers in the OBD (i.e. Birmaher, Goldstein, Axelson et al., 2013; Farchione, Birmaher, Axelson et al., 2007; Howes, Lim, Theologos et al., 2011), supporting the view that trait like dispositions impact the development of mood disorders.

To our knowledge there have been only a few studies comparing personality across affected and unaffected OBD. Farchione and colleagues (2007) found that independent of child psychopathology, OBD aged 6-18-years-old were rated by both themselves and their parents as being more irritable. BD parents also rated their children as being more hostile. When comparing the OBD who had developed BD to unaffected OBD and controls, Birmaher and colleagues (2013) found that the affected OBD evidenced the highest levels of irritability, followed by unaffected OBD, with controls showing the lowest amount of irritability, suggesting a possible prodromal marker to the disorder.

Unfortunately, very few studies have assessed the OBD using the "Five Factor Model," the current gold standard in personality profile assessment (Costa & McRae, 1992). Neuroticism, and to a lesser degree introversion, have been identified as traits which confer risk for mood disorders (Kendler, Gatz, Gardener, & Pedersen, 2006), perhaps in part due to increasing an individual's reactivity to stressful events (Bolger & Schilling, 1991). Understanding personality profiles in the OBD may give us clues as to how they navigate emotional/stressful and interpersonal situations. In general it is thought

that personality precedes psychopathology. However, this theory has been challenged (see Klein et al., 2002). Studying personality in a group of individuals at high risk of developing affective disorders but who have not yet developed a disorder would contribute well to this discussion.

1.2.8 Summary and conclusions from the literature on the OBD

To date, research on the OBD shows that they grow up in environments in which family functioning may be compromised. Along with being at greater genetic and environmental risk for the development of psychopathology, the OBD also exhibit risk factors in the form of maladaptive temperament and cognitions, compromised social functioning, behavior problems, neuropsychological deficits, and academic difficulties when compared to offspring of mentally well parents. However, much of the research on the OBD has focused on psychiatric outcomes, neuroimaging, and risk factors in childhood. Considerably less is known about the psychosocial contexts of the OBD as they move into young adulthood. Personality structure, patterns of stress coping, and engaging in high-risk behaviors are all factors that warrant further examination in this population. Furthermore, the development of effective interventions for OBD is partly dependent on understanding early mechanisms that contribute to the continuity of maladaptive development. Well-designed prospective longitudinal studies are a valuable source of information about risk and resiliency factors in high-risk populations (see Serbin & Karp, 2004). Such studies are able to take into account interacting factors such as environmental context, genetic vulnerability and individual growth and change, and identify factors that predict, mediate and moderate different developmental pathways.

1.3 Rationale and goals of the current study

The goals of this dissertation were twofold: 1) to provide a comprehensive assessment of non-psychiatric outcomes in the OBD (Study 1) and 2) to examine antecedents of sexual risk behavior (Study 2), a risk factor found in study 1. The first study assessed a sample of 148 OBD and offspring of parent with no mental disorder (controls) aged 14 to 27 years. This cross-sectional study aimed to contribute to the literature on the OBD by assessing psychosocial risk factors in the adolescents and young adult offspring, with particular focus on factors that contribute to the generation and maintenance of stress. The objectives of the first study were: (1) to examine differences in personality traits, coping style, and risk-taking behavior (smoking, antisocial behaviors, high risk sexual behaviors, self-injury, and suicidality) between the OBD and controls, and (2) to compare these psychosocial profiles in offspring who had developed an affective disorder with those who had not, so as to tease apart prodromal or vulnerability markers from those that are present by virtue of having an affective disorder. It was hypothesized that the OBD would report higher ratings of neuroticism and lower ratings of extraversion, more frequent use of maladaptive coping, and more risky behavior than control offspring, and that these differences would be present irrespective of having developed an affective disorder.

The first study was cross-sectional in nature, and as such was not able to contribute to our understanding of mechanisms or processes underlying the development of risk behaviors, namely sexual risk behaviors (SRBs). To this end, the second study attempted to position the results of study 1 within a developmental context. Specifically, we wanted to ascertain the extent to which problem behavior seen in adolescence showed continuity

with childhood problem behaviors and whether the development of these behaviors was influenced by parents' personality as measured in childhood. To this end, we assessed a longitudinal sample consisting of 132 offspring. Families were participants in a prospective longitudinal study of families with a parent diagnosed with BD or parents with no mental disorder. Offspring were assessed once at age 4-14 years and then again 10 years later.

The objectives of this study were threefold. First, we sought to ascertain the contribution of parents' personality traits of neuroticism, extraversion, agreeableness, conscientiousness, and openness to experience, as measured when their offspring were in middle childhood to the prediction of high-risk sexual behaviors in adolescence and early adulthood. The second objective was to determine the extent to which childhood problem behaviors mediate the association between parents' personality in childhood and SRBs. Finally, we sought to determine whether the associations between parents' personality and offspring behavioral outcomes would be stronger among the OBD than control offspring. Specifically, we assessed whether risk status would moderate the pathway between parents' neuroticism and childhood behavior problems and/or the pathway between childhood behavior problems and the subsequent development of SRBs. Based on our previous research in this area (Ostiguy et al., 2012), we hypothesized that parents' neuroticism would predict high-risk sexual behaviors in offspring. Furthermore, because there is a large body of research linking SRBs with externalizing problems (i.e. Caminis et al., 2007; Donengen et al., 2003), we hypothesized that the relationship between parents' neuroticism and offspring SRBs in late adolescence and early adulthood would be mediated by children's externalizing problems, but not internalizing problems, in

middle childhood. Lastly, it was expected that these associations would be more robust in the OBD than the offspring of parents with no affective disorder (i.e. moderated mediation). Taken together, this research could elucidate risk pathways to dysfunction in the OBD and provide guidance for the development of preventative interventions in BD families.

CHAPTER 2. STUDY 1, MANUSCRIPT 1: PERSONALITY, COPING, RISKY BEHAVIOR, AND MENTAL DISORDERS IN THE OFFSPRING OF PARENTS WITH BIPOLAR DISORDER: A COMPREHENSIVE PSYCHOSOCIAL ASSESSMENT

2.1 INTRODUCTION

Bipolar disorder (BD) is among the top 10 most burdensome medical conditions worldwide (Murray & Lopez, 1997; WHO, 2001). It is associated with marked psychosocial dysfunction, including high rates of impulsive behavior such as suicidality (Tondo et al., 1998), substance abuse (Weissman, Bland, Canino et al., 1996), hypersexuality (Adelson, Bell, Graff et al., 2013), and criminal behavior (Soyka & Zingg, 2010; Swann et al., 2011). Furthermore the offspring of parents with bipolar disorder (OBD) are at greater risk of developing maladaptive development (see Jones & Bentall, 2008), likely by virtue of inherited traits combined with sub-optimal rearing environments (Rutter, 2009). There is substantial evidence of psychopathology among the OBD (i.e. Birmaher, Axelson, Monk, Kalas, Goldstein, Hickey et al., 2009; Duffy, Alda, Hajek, Sherry, & Grof, 2010; Henin, Biederman, Mick, et al., 2005; Hillegers, Reichart, Wals, et al., 2005; LaPalme, Hodgins, & LaRoche, 1997; Vandeleur, Rothens, Gholam-Rezaee, et al., 2012). Rates of affective disorders have been estimated at 15-56% in adolescent and young adult OBD, compared to 0-12% in control samples (Birmaher et al., 2009; Duffy et al., 2006; Henin et al., 2005; Hillegers et al., 2005; Hirshfeld-Becker et al., 2006; Mesman, Nolen, Reichart et al., 2013; Vandeleur et al., 2012). In children, rates of disruptive behavior disorders and anxiety disorders are roughly two to nine times those observed in controls (Birmaher et al., 2009; Hirshfeld-Becker et al., 2006; Vandeleur et al., 2012). Recent clinical staging models suggest that the OBD are likely to

display different age-specific internalizing and externalizing pathologies (Duffy, et al., 2010, Klimes-Dougan, Long, Lee, et al., 2010), suggesting an underlying vulnerability that manifests in different symptom presentation across development. Most research on the OBD has focused on rates of psychopathology while few studies have examined personality and non-psychiatric psychosocial risk factors in the OBD.

Personality and psychopathology have been inextricably linked, although the exact nature of this relationship has been debated (see Widiger, Verheul, & van den Brink, 1999). In our model of the OBD (Ellenbogen and Hodgins, 2004; Ostiguy, Ellenbogen, & Hodgins, 2012), we hypothesized that one marker of the genetic vulnerability for mood disorders is high levels of the trait of neuroticism (Fanous et al., 2002) - a tendency to react emotionally to stressors and daily hassles. Being raised by one or two parents who themselves model over-reactivity to daily hassles and ineffective coping with stress may compromise the ways in which their offspring cope with life stress. The parents' neurotic behavior creates a family environment that is stressful, chaotic, and unpredictable (Chang, Blasey, Ketter, & Steiner, 2001; Ellenbogen & Hodgins, 2004), and these parents fail to provide adequate support and structure for their children (Ellenbogen & Hodgins, 2009). It has been postulated that the family environment and parenting practices, in interaction with a genetic vulnerability, lead to deficits in emotional and behavioral regulation among the children (Derryberry & Rothbart, 1997; Ellenbogen & Hodgins, 2009; Loman & Gunnar, 2010). In sum, these adverse family-environmental effects associated with high neuroticism in parents, are postulated to elicit a number of subsequent environmental outcomes that have a negative

impact on offspring. These negative impacts include a high sensitivity and inability to effectively cope with stress, dysregulated behavior, and high neuroticism.

Consistent with the model, there is evidence that the OBD, relative to control offspring, experience more moderate to severe stressful life events (Ostiguy et al., 2009), display a greater biological sensitivity to stress (Ostiguy et al., 2011), and exhibit a ruminative coping style (Jones et al., 2006). Furthermore, for those who go on to develop a disorder, stressful life events are likely to precede onset of the disorder (Petti, Reich, Todd, Joshi, Galvin, Reich, et al., 2004; Duffy, et al., 2007). As such, it would seem that the OBD are not only more prone to experience stress in their lives, but also may experience or cope with stress differently than others. In a recent longitudinal study of the OBD, it was found that high neuroticism in parents, as measured when the offspring were aged 4-14, predicted poor interpersonal functioning in their offspring at 10-year follow (Ostiguy et al., 2012). The association between parents' personality and interpersonal functioning in offspring was mediated by offspring's internalizing behavior problems in middle childhood. Although this study was consistent with our model, little is known of the personality profiles of the OBD, nor about their coping or risky behaviors in late adolescence and early adulthood.

Health-related risk behaviors, such as criminality, risky sexual behavior, and suicidality, have rarely been studied in the OBD. These are important because, as adolescents take an active role in shaping and selecting their environments, they may create stressful circumstances for themselves in the form of impulsive or risk-taking behavior. Such behavior is particularly likely in the OBD, who display higher levels of sensation seeking (Nurnberger, Hamovit, Hibbs, et al., 1988), a trait associated with the

development of delinquent behavior (Harden, Quinn, & Tucker-Drob, 2012), as well as externalizing problems (Linnen, aan het Rot, Ellenbogen, & Young, 2009). Moreover, there are important links between the endorsement of behaviors such as illicit drug use, smoking, high-risk sexual behavior, and criminality and increased risk of developing a mental disorder (Fergusson, Horwood, Swain-Campbell, 2002; Lahey, Loeber, Burke, & Applegate, 2005). To the best of our knowledge, there is only one study that directly addresses risk-taking in the OBD. Jones, Tai, Evershed, Knowles and Bentall (2006) found that OBD who had developed an affective disorder were more likely to endorse a response style indicative of general risk taking than OBD who had not developed an affective disorder, as well as unaffected controls. However, no study to date has explored specific sexual, health-related, and criminal risk taking behaviors in this population.

In contrast to studies of mental health in the OBD (i.e. Goldstein, Shamseddeen, Axelson, Kalas, Monk, Brent et al., 2010; Hillegers et al., 2005), the present study focused on *non-psychiatric* outcomes, in addition to the rates of affective and non-affective disorders among high-risk offspring. The objectives of the current investigation were twofold: (1) to examine differences in personality traits, coping style, and risk-taking behavior (smoking, antisocial behaviors, high risk sexual behaviors, self-injury, and suicidality) between the OBD and controls, and (2) to compare these psychosocial profiles in offspring who have developed an affective disorder with those who have not, so as to tease apart prodromal markers from those that are present by virtue of having an affective disorder. It was hypothesized that the OBD would report higher ratings of neuroticism and lower ratings of extraversion, more frequent use of maladaptive coping,

and more risky behavior than control offspring, and that these differences would be present irrespective of having developed an affective disorder.

2.2 Method

Participants

Participants included 148 (65 female, 83 male) offspring between the ages of 14 and 27 years (M = 19.38; SD = 3.56) from 91 families (71 OBD, 77 control). The sample was comprised of two cohorts recruited at different times. One hundred and thirty three of the offspring (80 families; 86.5 % of the full sample) were participants of an ongoing prospective longitudinal study of families with a parent diagnosed with BD or parents with no mental disorder. A small number of offspring were recruited more recently in an effort to increase the sample size (15 offspring [6 OBD, 9 controls] from 11 families (4 OBD, 7 controls); 9.9 % of the total sample).

Families in the longitudinal study were recruited between 1996 and 1998. Inclusion criteria for entry into the longitudinal study were (a) adults raising at least one biological child between the ages of 4 and 14, b) fluency in either English or French, and c) children being raised and educated in Canada. Families in which either a parent or child had a chronic physical disease or handicap, and/or an IQ below 70, was excluded. Parents with a diagnosis of BD and their families were recruited from psychiatric outpatient clinics in the province of Québec, as well as from advocacy and support groups. Families in which parents had no mental disorder were recruited from the same neighborhoods as the families with BD, through physicians' offices and community organizations. Detailed demographic and psychosocial information on the original sample

is described in Ellenbogen and Hodgins (2004). The new cohort was recruited through advertisements in local newspapers in 2006-2007. Inclusion and exclusion criteria were the same, except for the age requirement for offspring, which was set at 13 to 23 years of age in order to match the age of the existing cohort. Informed consent was obtained from all participants.

All parents were assessed using the Structured Clinical Interview for *DSM-III-R* (SCID-I; Spitzer, Williams, Gibbon, & First, 1992). Parents from the control families had no current or lifetime axis-I disorder, except for past episodes of substance abuse, anxiety disorders, or eating disorders, as indicated by the SCID-I. Eighteen percent of the OBD and 17% of the controls who were originally part of the longitudinal study refused to participate or were not located for the current assessment. Children who did not participate were compared to those who did on measures of problem behavior and IQ assessed during middle childhood. No significant differences were found among the groups. One OBD participant failed to complete their questionnaires and six returned personality questionnaires that were incomplete. Nine control participants failed to complete their questionnaires (N = 6) or returned incomplete personality questionnaires (N=3).

Measures

Diagnostic Assessments

The Structured Clinical Interview for *DSM-IV-R* (SCID-I; First, Gibbon, Spitzer, & Williams, 1992) and Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL; Kaufman, Birmaher, & Brent, Rao, Flynn, Moreci, et al.,1997) were used to assess adult and adolescent offspring, respectively.

Interviews were conducted by licensed clinicians and doctoral students who were trained and supervised in the use of the official French version of the SCID-I (Laboratoire de Psychogénétique Moléculaire du Centre Hospitalier, l'Université de Laval). The inter-rater agreement for affective disorders obtained on 15% of the SCID-I and K-SADS-PL interviews was excellent ($\kappa = 0.82$).

Personality

Participants 19 years or older (n=74) completed the *revised NEO Personality Inventory* (NEO-PI-R, Costa & McRae, 1992). This five-factor personality inventory includes 240 items that assess neuroticism, extroversion, agreeableness, openness, and conscientiousness. High internal consistency, with coefficients ranging from .89 to .95, and temporal stability over 6 years has been reported for the NEO-PI-R (Costa, Herbst, McCrae, & Siegle; 2000; Costa & McCrae, 1992; Rolland, Parker, & Stumpf, 1998). Excellent psychometric properties have been demonstrated with the French translation (Rolland et al., 1998). Participants who were 18 years of age or younger (n=58) completed the *Junior Eysenck Personality Questionnaire (EPQ;* Eysenck & Eysenck, 1985). The EPQ evaluates four main traits in adolescence: neuroticism, extraversion, psychoticism, and delinquency. In this study, measures of neuroticism and extraversion were created by combining standardized, via z-distribution, NEO-PI-R and EPQ data. Although the composition of the NEO-PI-R and EPQ differ, they measure similar personality dimensions (Enns & Cox, 1997). A measure of impulsivity was created by combining standardized scores from a 25-item impulsiveness scale (Le Blanc, McDuff, Frechette, Langelier, Levert, & Trudeau-Blanc, 1997; 18 years or younger) and the NEO-PI-R impulsiveness facet.

Coping Inventory for Stressful Situation—Adult and Adolescent Versions (CISS).

Offspring completed the adult (for those over 18 years of age) or adolescent (for those 18 years old and younger) version of the CISS（Endler & Parker, 1990）. The CISS includes 48 items and yields standardized *T* scores for task-oriented, emotion-focused, and avoidance-oriented strategies, including distraction. Support for the factor structure of the CISS, as well as the reliability and validity of the measure, has been found in clinical (McWilliams, Cox, & Enns, 2003) and general populations (Endler & Parker, 1990).

Assessment of psychosocial risk

An in-house structured assessment, administered by a licensed clinician or trained senior graduate student in clinical psychology, was used to assess past and present suicidal thoughts and behaviors, self-injury, smoking habits, risky sexual behaviors, and criminal behavior.

Suicidal behavior was defined by the presence of suicidal ideation and/or suicidal behavior. This definition has been used effectively in past studies (see Meyer, Salzman, Youngstrom, Clayton, Goodwin, Mann, et al., 2010). Participants in this category (N = 40) had positively endorsed having had considered suicide, having had a plan to commit suicide, having a real intention to go through with the suicide, and/or having had failed suicide attempts.

Self-injury was defined as physically inflicting harm on oneself (tissue damage) with the intention of releasing tension rather than ending one's life. Self-harm could include, but was not limited to cutting, burning, scratching, or dripping corrosive

substances onto one's skin. Similar definitions of self-injury have been reliably used in the self-harm literature (Gratz, 2001; Yates, 2004).

Regular smoking was defined as smoking more than 5 cigarettes a day, which was based on norms from a recent national survey of smoking behavior in American high schools (Jones, Kann, & Pechacek, 2011).

High-risk sexual behavior consisted of risky sexual practices. It was defined as having had unprotected sex, an abortion, or sex before the age of 16 years. The measurement of sexual risk behaviors is consistent with other studies in this area (see Buhi & Goodson, 2007; Charles & Blum, 2008 for reviews). The age criterion for early sex initiation was based on studies showing that sex before the age of 16 years is linked to maladaptive developmental outcomes (Spriggs & Halpern, 2008a; Spriggs & Halpern, 2008b; Madkour, Farhat, Halpern, Godeau, & Gabhainn, 2010).

Criminal behavior was defined as the self-report of the following: committing an act of vandalism, being physically violent with another person, committing theft, any illegal infraction while driving (i.e., excessive speed, reckless driving etc.), or selling illegal substances.

Procedure

Participants gave written consent, and parental consent was obtained for those 17 years of age or younger, and then took part in a three-hour assessment at the university. They underwent a diagnostic interview, an assessment of psychosocial risk factors, and an assessment of episodic and chronic stress (not reported here, see Ostiguy et al, 2009). Participants then underwent computer-based information processing tasks (data not reported here), and completed questionnaires. Participants received an honorarium of

$150 CAN for participating in the current wave (10-year longitudinal follow-up) of data collection. All procedures were approved by the Human Research Ethics Committee of Concordia University.

Data Analyses

Data were screened for outliers, defined as scores at least three standard deviations from the mean, and violations of normality. One participant's task-oriented coping score was identified as an outlier. Analyses were performed with and without this participant's data and, as results did not differ, we included this participant in the analyses.

Data analyses were conducted in three parts. First, the OBD were compared to control offspring on indices of personality, coping, and high-risk behavior using a Sex X Group (OBD, control) multivariate analyses of covariance (MANCOVAs). Age was included as a covariate. Non-parametric tests (chi-square) were used to assess group differences in suicidal behavior, smoking, risky sexual behavior, criminal behavior, or driving infractions, all coded as dichotomous variables (present/absent).

Second, to determine whether differences observed in the first set of analyses of personality and coping were related to the presence of an affective disorder or risk status, we repeated the above MANCOVAs comparing offspring with an affective disorder (N = 33; 73% of whom were OBD), OBD without an affective disorder (N = 50), and controls without an affective disorder (N = 65). Age and the presence of a current co-morbid non-affective disorder (N = 3; 2 OBD, 1 control) were added as covariates in these analyses.

Third, to determine whether observed differences in dichotomous variables were related to the presence of an affective disorder or risk status, binary logistic regression

was used to compare the effect of risk status versus the presence of an affective disorder on dichotomous outcomes. Age and sex of the participant were entered in the first step of the regression, followed by risk group status and presence of an affective disorder. For analyses of high-risk sexual behavior, having had a significant romantic relationship in the last year was also entered as a predictor in the second step, to control for this potential confound. Wald's criterion was used to assess the significance of the odds ratios. All statistical analyses were conducted using SPSS version 20.0**.**

When siblings were used in data analyses, it introduces the possibility of violating the independence assumption among offspring data. As such, analyses were conducted with and without siblings (using random deletion) to determine if the inclusion of siblings may have biased the results. These findings did not differ across these analyses. As such, we included all participants in the analyses.

2.3 Results

Mental Health Outcomes

Rates of mental disorders in the full sample are presented in Table 1. Twenty-three (31.1 %) of the OBD and 7 (9.5%) of controls were diagnosed with a lifetime affective disorder, and 42 (56.8 %) OBD and 24 (32.4 %) controls were diagnosed with a lifetime non-affective disorder.

Among the **longitudinal cohort** followed for approximately 10 years since the age of 4 to 14 years (n=128), 44 (65.7 %) of the OBD met diagnostic criteria for at least one mental disorder, compared to 28 (41.2%) of the controls. Twenty-two (32.8%) of the OBD met criteria for an affective disorder compared to 8 (11.8%) of controls; 38 (56.7%) of OBD met criteria for a non-affective disorder compared to 22 (34.2 %) of controls. In

terms of specific diagnoses, 2 (3.0 %) of OBD met criteria for BD-I, and 1(1.5%) met criteria for BD-II, and no controls met criteria for BD. Eighteen (26.9%) of OBD had had a major depressive episode to date, compared with 7 (10.3%) of the controls, anxiety disorders were diagnosed in 20 (29.9%) of OBD and 13 (19.1%) of controls, whereas 22 (32.8%) of OBD met criteria for a lifetime externalizing disorder, compared to 13 (19.1%) of controls.

Personality

A Sex X Group MANCOVA on standardized scores for neuroticism, extraversion, and impulsiveness revealed no significant main effect of group or interaction (see Table 2). Data from the NEO-PI-R (N= 74) and EPQ (N = 58) were also analyzed separately in order to determine whether there were group differences on the separate measures, reflecting age- and/or content-related differences. The analyses did not yield significant main effects of group on neuroticism, extraversion, or impulsiveness (data not shown). Analyses were repeated comparing offspring with an affective disorder, unaffected OBD, and unaffected controls (see Table 3). Again, no significant group or sex differences were found. In sum, no group differences in personality were detected.

Coping

A Sex X Group MANCOVA was conducted on task-oriented, emotion-oriented, avoidance, and distraction coping scores. Significant main effects of group [Wilk's λ = .83, $F(1, 136) = 6.92$, $p<.01$; see Table 2] and sex [Wilk's λ = .92, $F(1, 136) = 2.83$, $p< .05$] were found. The OBD used fewer task-oriented coping strategies ($F(1, 136) = 9.99$, $p< .01$) and more distraction coping strategies ($F(1, 136) = 8.11$, $p< .05$) than controls. Female participants were more likely to endorse emotion-oriented coping ($F(1, 136) =$

7.38, p<.00) and avoidant responses to stress than male participants (F (1, 136) = 5.56, p<. 05). Furthermore, a Sex X Group interaction was observed [Wilk's λ = .94, F (1, 136) = 2.19, p = .07], although it fell short of conventional statistical significance. A follow-up analysis using univariate ANOVAs revealed that female OBD (42.41 ± 11.31) tended to endorse more emotion-oriented coping than male OBD [34.56 ± 10.28; F(1,69) = 11.39, p<.01], and this sex difference was not observed among the controls [females: 40.53 ± 8.78; males: 39.41± 11.63; F(1,68) = .150, p = .70]. No interactions were observed for other coping scales (data not shown).

Next, a MANCOVA was conducted to determine group differences in coping styles for offspring with an affective disorder relative to OBD and controls without an affective disorder (See Table 3). Significant main effects of group [Wilk's λ = .84, F (1, 133) = 3.06, p<.01] and sex [Wilk's λ = .92, F(1, 133) = 2.87, p<.05] were found (see Table 3). Post-hoc Tukey HSD tests revealed that offspring with an affective disorder used significantly more emotion-oriented coping than OBD with no affective disorder (p <.01) and controls (p<.05), but the latter two groups did not differ in emotion-oriented coping. In sum, the OBD reported using less task-oriented and more distraction coping. Emotion–oriented coping was highest amongst female OBD, and the relationship between emotion-oriented coping and risk status was explained, in part, by the presence of a lifetime affective disorder.

High Risk Behavior:

Suicidal Behavior

Chi square analyses were conducted on measures of suicidal behavior, smoking, high-risk sexual behavior, infidelity, and criminal behavior (see Table 2). Although there

were no group differences between OBD versus controls, suicidal behavior was more prevalent in the offspring with affective disorders than the OBD with no affective disorder and controls (See Table 3). The latter two groups, however, did not differ from each other in suicidal behavior.

Smoking

A non-significant trend suggested that a higher percentage of OBDs endorsed regular smoking when compared to controls (see Table 2). The offspring with affective disorders were also more likely to smoke than OBD with no affective disorder and controls, although this effect fell short of conventional statistical significance (see Table 3). The latter two groups, however, did not differ from each other in smoking.

High-risk sexual behavior

The proportion of offspring reporting high-risk sexual practices was significantly greater in OBD than controls (see Table 2). A greater proportion of offspring with an affective disorder (57.6 %) and OBDs with no history of affective disorders (58%) endorsed high-risk sexual behavior than controls with no affective disorder (35.4%; $\chi^2 = 7.36$ df = 1, p = .016; see Table 3). Acts of infidelity did not differ between the groups.

Post-hoc analyses were conducted on the items that made up the risky sexual behavior measure. The OBD reported more unprotected sex (35 OBD [49.29%]; 23 controls [29.91%]; χ^2 [1, N = 148] = 5.85 $p < .05$) than controls. They did not, however, report significantly more abortions (OBD [6, 12.83%]; controls [5, 7.04%]; χ^2 [1, N= 148] = .03 p = .86), or significantly more early initiation (25 OBD [35.21%]; 18 controls [23.38%]; χ^2 [1, N = 148] = 2.51, p = .11) than the control offspring. Affected offspring

were more likely to endorse unprotected sex (18, 54.5%) than unaffected OBD (21, 42%) and controls (19, 29.2%; χ^2 [1, N = 148] = 6.14, $p < .05$).

Antisocial behavior

There were no significant differences seen in the proportions of OBD and controls who reported participating in acts of violence, vandalism, drug-dealing, or who had been in contact with the police for a driving related infraction (see Table 2). The same was true for the proportions of offspring with and without affective disorders (see Table 3).

Factors Associated with High Risk Behaviors

Six separate sequential logistic regressions were carried out to determine the probability of engaging in suicidal behavior, smoking, high-risk sexual behaviors, and antisocial behavior based on group status and/or presence of affective disorder (see Table 4). Controlling for age and sex, it was found that having an affective disorder increased the likelihood of reporting suicidal behavior (Wald = 15.23, 1 df; $p< .001$), and having a parent with BD predicted an increased likelihood of engaging in risky sexual behavior (Wald = 4.13, 1 df; $p < .05$). We repeated the logistic regression predicting risky sexual behavior while controlling for the presence of substance abuse or dependence and externalizing disorders, both of which could explain this relationship. The addition of these variables to the model had negligible effects on the relationship between having a parent with BD and risky sexual behavior (data not shown). Logistic regressions assessing smoking, criminal behavior, and infidelity did not yield significant results.

2.4 DISCUSSION

In this study, we conducted a comprehensive assessment of mental health, personality and psychosocial risk factors in adolescent and young adult OBD and

controls. Similar to other studies (Mesman et al., 2013; Duffy et al., 2010), rates of major depressive disorder (26.9%), BD (4.5%), and non-affective disorders (56.7%) were significantly elevated in the OBD relative to the controls. With regards to psychosocial factors, the central finding was that the OBD were more likely to engage in sexual risk behaviors (SRBs) than the controls. Risky sexual behavior may represent a particularly important psychosocial marker of risk among the OBD because it was found independent of having an affective disorder. The OBD also reported less task-focused coping and more distraction-focused coping than controls. Female OBD had a tendency to be more likely to endorse the use of emotion-oriented coping than high-risk males and controls. All of the above findings, except for high-risk sexual behavior, could be attributed in part to the fact that the OBD have higher rates of affective disorder than the controls. Surprisingly, OBD did not differ from controls on measures of personality.

As hypothesized, the OBD were more likely to engage in risky sexual behavior, as indexed by initiating sexual activity before the age of 16, having had at an abortion, or engaging in unprotected sex. In general, adolescent SRBs are thought to be related to deficits in core competencies including positive sense of self (self-efficacy; self-esteem), self-regulatory capacities, decision-making skills, and prosocial connectedness (see Charles & Blum, 2008). There are several possible explanations for the elevated rates of SRBs seen in the OBD relative to controls. First, the OBD appear to exhibit disproportionate rates of externalizing or sensation seeking behaviors (i.e. Carlson & Weintraub, 1993; Nurnberger, Hamovit, Hibbs, et al., 1988). A prominent theory regarding SRBs suggest that they are an extension of externalizing problem behavior (Meyer-Bahlburg, Dolezal, Wasserman, & Jaramillo, 1999; Jessor & Jessor, 1977),

evidenced by links to a past history of conduct disorder (Emery, Waldron, Kitzmann, & Aaron, 1999; Woodward & Fergusson, 1999), as well as future engagement in delinquent activities (Armour & Haynie, 2007; Leitenberg & Saltzman, 2000). Moreover, in the Dunedin Longitudinal study, conduct disorder in males and behavioral problems at school in females independently predicted early initiation of sexual activity after controlling for a number of factors including age, SES, and family variables (Paul, Fitzjohn, Herbison, & Dickson, 2000). There is evidence that risky sexual behavior is propagated by genetically influenced externalizing traits (Bricker, Stallings, Corley, Wadsworth, Bryan, Timberlake et al., 2006; Donahue, D'Onofrio, Lichenstein, & Langstrom, 2013; Dunne, Martin, Statham, Slutske, Dunwiddie, Bucholz, et al., 1997). That is, the co-occurrence of sexual activity and delinquency seen in the general population may be due to common genetic influences related to personality traits such as sensation seeking and impulsivity (Verweij, Zietsch, Bailey, & Martin, 2009). As such, the OBD could be prone to such disruptive behavior by virtue of an inherited tendency towards externalizing behaviors.

Secondly, adolescent SRBs are influenced by family factors including parental support, monitoring, and control (i.e. Capaldi, Stoolmiller, Clark & Owen, 2002; Price & Hyde, 2009), as well as high levels of family conflict (Ary, Duncan, Duncan & Hops, 1999). There is evidence that the OBD grow up in environments that are unstable, disorganized, and characterized by high conflict (Belardinelli, Hatch, Olvera, et al., 2008; Chang et al., 2001; Chang, Steiner, & Ketter, 2000; Romero, Delbello, Soutullo, Stanford & Strakowski, 2005). Furthermore, parents with BD are more likely than controls to engage in poor parenting practices (Ellenbogen & Hodgins, 2004). As such, it may be the

case that the OBD are at risk of developing problem behaviors such as SRBs by virtue of their home environment.

Finally, previous studies in the OBD have found evidence of both greater reactivity to interpersonal stressors in the natural environment (Ostiguy et al., 2011) and enduring difficulties in interpersonal interactions (Linnen et al., 2009; Ostiguy et al., 2009). It is possible that SRBs may represent an outgrowth of interpersonal difficulties. For example, Halpern, Campbell, Agnew, Thompson, and Udry (2002) found that males who showed greater stress reactivity to a range of laboratory social stress tests were less likely to use condoms on a regular basis. The authors interpreted this as an avoidant reaction to the potentially anxiety-provoking interpersonal negotiation of condom use. In young women, high levels of stress and low social support have been shown to be predictive of SRBs and sexually transmitted infections (Mazzaferro, Murray, Ness, Bass, Tyus, & Cook, 2006). Perhaps, the OBD have difficulty with limit setting and the negotiation of safe sex in their sexual relationships, and that this may be due in part to psychological and biological sensitivity to interpersonal stress. Given the deleterious effects that SRBs can have on physical and psychological health (i.e. Langille, Asbridge, Kisley, & Wilson, 2012; Rubin, Gold, & Primack, 2009), such propagating factors warrant further investigation in OBD populations.

It is noteworthy that hyper-sexuality is often a key symptom (excessive involvement in pleasurable activities) of BD (APA, 2013). Heightened sexual behavior is evidenced more often in individuals with BD, relative to unipolar and control populations (Dell'Osso, Carmassi, Carlini, Rucci, Torri, Cesari, et al., 2009). In fact, hypersexuality has been suggested as an important factor in differentiating early onset BD from other

externalizing pathology such as attention-deficit hyperactivity disorder (Adelson et al., 2013). Although a recent study demonstrated a positive relationship between elevated symptoms of mania and high-risk sexual behavior in adolescents (Stewart, Theodore-Oklota, Hadley, Brown, Donenberg & Diclemente, 2012), no studies to date have reported on sexual behavior in prodromal or OBD populations.

The present findings regarding coping strategies add to the scarce literature of dysfunctional coping styles in the OBD (i.e. Bentall, Myin-Germeys, Smith et al., 2011; Jones et al., 2006), and are consistent with studies of coping in patients with MDD and BD (Rohde, Paul, Lewinsohn et al., 1990; Palickova, Vareses, Smith et al., 2013). Poor stress coping has been proposed as one of the mechanisms that elevates risk for developing psychopathology in at-risk youth (Langrock, Compas, Keller, Merchant, & Copeland, 2002). Stress-coping may be particularly important in the OBD as studies have shown that they are exposed to more negative stressful life events (Ostiguy et al., 2009) and are more biologically sensitive to stress than are controls (Deshauer, Grof, Alda, et al., 1999; Ellenbogen et al., 2006; Ostiguy et al., 2011).

The hypothesis that the OBD would display higher mean levels of neuroticism and impulsivity and differ from controls on levels of extraversion was not supported. The only other study of the five-factor model of personality in the OBD revealed a similar lack of association (Rothen et al., 2009). One reason for these null findings is the age range of the sample. Personality traits are unstable, therefore less consistently detectable, prior to adulthood. Indeed, it has been argued that personality changes continue through young adulthood, reaching relative stability at age and 30 and older (Costa & McRae, 1992; Lucas & Donnellan, 2011; Specht, Egloff, & Schmukle, 2011). Importantly, there

is evidence to suggest that personality is susceptible to change in response to consequential life events and experiences (Ormel, Riese, & Rosmalen, 2012; Specht et al., 2011). Indeed, affected OBD, were more likely to display high neuroticism when compared to unaffected OBD and controls, supporting the "scar" hypothesis that personality changes follow mood episodes (Rothen et al., 2009).

There are a number of limitations in the present study that warrant discussion. Lifetime rates of externalizing disorders in this sample were underestimated due to the use of the SCID-I in participants 18 years of age and older, which does not assess for externalizing disorders. Future research in this area should assess the relation between externalizing problems, including substance use, and SRBs across development. Similarly, the present study did not include a sensitive measure of hypomanic symptoms. Given the prominence of hypersexuality in BD, SRBs may have important implications in the development of BD. The broad age range in this study suggests that some findings (i.e. risk behaviors) may be less meaningful among younger participants relative to older ones. Furthermore, the sample consists of offspring from two different recruitment phases. Although there may be important differences between the subsamples, the small size of the newer sample precludes our ability to statistically assess the magnitude of these differences (besides descriptive statistics). Finally, personality was measured using a composite of two separate, age-appropriate measures (the EPQ and the NEO-PI-R). Although these two scales have shown good convergent validity with one another (Costa & McRae, 1995), the use of a composite measure may have precluded our ability to find meaningful group differences.

Taken together, the results of the current study complement a large body of research on mental health outcomes in the OBD (i.e. Birmaher et al., 2010). Of note, SRBs and coping skills among the OBD may represent a key developmental risk factor that warrants further attention. The identification of such risk factors is important to the understanding of the etiology of affective disorders (Rutter, 2009), particularly in the context of gene-environment interplay, and could provide important targets for intervention among high-risk youth during adolescence.

Table 1. Lifetime Diagnoses in study participants

	OBD		**Controls**		
N	71		77		
Age (years) ± SD	20.5 ± 3.2		19.2 ± 3.4		
	Freq. (%)		Freq. (%)		χ^2
Lifetime Diagnosis (any)	48 (64.9%)		30(40.5 %)		***8.78*** **
	Current	**Past**	**Current**	**Past**	
Mood Disorders	6 (8.1%)	17 (22.9%)	0	8 (10.7%)	10.21**
Major Depressive Disorder	1 (1.3%)	17 (22.9%)	0	8 (10.7%)	
Bipolar Disorder I	2 (2.7%)	0	0	0	
Bipolar Disorder II	2 (2.7%)	0	0	0	
Anxiety Disorders	22 (29.7%)	5 (6.7%)	4 (5.3%)	9 (12%)	3.50t
Social Phobia	5 (6.7%)	1 (1.3%)	0	2 (2.7%)	
Specific Phobia	8 (10.8%)	1 (1.3%)	2 (2.7%)	7 (9.5%)	
Generalized Anxiety Disorder	6 (8.1%)	0	2 (2.7%)	0	
Post Traumatic Stress Disorder	0	2 (2.7%)	0	0	
Obsessive-Compulsive Disorder	0	1 (1.3%)	0	0	
Panic Disorder/Agoraphobia	3 (4.1%)	0	0	0	
Externalizing Disorders	14 (18.9%)	15 (20.3%)	7 (9.5%)	10 (13.3%)	4.21*
Substance Use Disorders	11 (14.9%)	13 (17.6%)	6 (8.0%)	7 (9.5%)	
Attention Deficit Hyperactivity Disorder	2 (2.7%)	0	1 (1.3%)	0	
Conduct Disorder/Oppositional	1 (1.3%)	2 (2.7%)	0	3 (4.0%)	

Defiant Disorder				
Other *	1 (1.3%)	6 (8.1%)	2 (2.7%)	5 (6.7%)

OBD: Offspring of parents with bipolar disorder

* Other diagnoses included past tic disorders (N = 3), current tic disorders (N = 1), past enuresis (N = 4), schizoaffective disorder (N = 1), past phencyclidine (PCP)-induced psychosis, (N = 1), current anorexia nervosa (N = 1), past adjustment disorder with depressive symptoms.

Table 2. Comparison of Offspring of Parents with Bipolar Disorder (OBD) and Controls on Psychosocial Risk Factors

	OBD	**Controls**	***Statistical Analysis***
	(M ± SD)	(M ± SD)	*F*
Personality (Collapsed Scores)			
N	64	68	----
Neuroticism	.11± 1.0	-.12± 1.0	1.70
Extraversion	.06± 1.1	-.13± .94	2.09
Impulsivity	1.76± 2.74	2.68± 2.83	.32
Stress Coping			
N	70	71	----
Task	52.91 ± 8.89	56.39 ± 7.91	9.99**
Emotion	38.15 ± 11.17	39.94 ± 10.31	0.06 [b]
Avoidance	46.77 ± 8.95	47.19 ± 10.07	0.24
Distraction	22.27 ± 5.67	20.25 ± 5.57	8.11**
High Risk Behaviors			
N	71	77	----
	Freq(%)	***Freq(%)***	χ^2
Smoking	29 (40.8%)	20 (26.0%)	3.69t
Risky Sexual Behavior [a]	43 (60.5%)	28 (36.4%)	8.67**
Suicidal Behavior	22 (31.0%)	18 (23.4%)	1.08
Self-Injury	5(7.0%)	3 (3.8%)	0.72

Antisocial behavior [a]	31 (43.6%)	25 (32.5%)	1.97

OBD: Offspring of parents with bipolar disorder; ONAD: Offspring of parents with no affective disorder.

[a] Risky sexual behavior = early initiation of sex, frequent unprotected sex, and/or having had an abortion; Anti-social behavior = trouble with the law involving driving infractions, violence, vandalism and/or drug dealing

*$p < 0.05$; **$p < 0.001$, [b] Group x Sex interaction, t non-significant trend,

Table 3. Comparison of Offspring With Affective Disorders to Offspring of Parents with Bipolar Disorder and Controls Without Affective Disorders on Psychosocial Risk Factors

	Offspring w/ affective disorder	**OBD (no disorder)**	**Controls (no disorder)**	***Statistical Analysis***
	M ± SD	M ± SD	M ± SD	*F*
Personality (Collapsed Scores)				
N	31	45	*56*	----
Neuroticism	.11 ±1.03	.07 ±1.09	-.14 ±.90	0.66
Extraversion	-.14 ±.98	.11 ±1.10	-.04 ±.96	1.55
Impulsivity	.11 ±.83	.19 ±.88	.09 ±.89	0.24
Stress Coping				
N	32	50	59	----
Task	52.95 ±9.98	54.40 ±8.62	55.81±7.60	2.01
Emotion	45.19 ±11.75	35.36 ±9.14	38.86 ±10.09	5.03** [b]
Avoidance	48.59 ±9.99	45.84 ±8.98	47.08 ±9.68	.26
Distraction	22.25 ±6.26	21.70 ±5.61	20.34 ±5.39	1.89
High Risk Behaviors				
N	33	50	65	
	Freq(%)	***Freq(%)***	***Freq(%)***	χ^2
Smoking	16 (48.5%)	18(36.0%)	15 (23.1%)	6.67t
Sexual Risk Behavior [a]	19 (57.6%)	29 (58.0%)	23 (35.4%)	7.36*
Suicidal Behavior	19 (57.6%)	8 (16.0%)	13 (20%)	20.33 ***
Self-Injury	3 (9.0%)	2 (4.0%)	3(4.6%)	1.15

Anti-social behavior [a]	13 (39.4%)	23 (46.0%)	20 (30.8%)	2.83

OBD: Offspring of parents with bipolar disorder

[a] Risky sexual behavior = early initiation of sex, frequent unprotected sex, and/or having had an abortion; Anti-social behavior = trouble with the law involving driving infractions, violence, vandalism and/or drug dealing

*$p < 0.05$; **$p < 0.001$, [b] Group x Gender interaction, t non-significant trend,

Table 4. Logistic Regression Predicting the Likelihood of Engaging in High Risk Behaviors (N = 148)

	PREDICTOR VARIABLES				
		Sex	Risk Status	Affective Disorder	Romantic Rel. (lifetime)
OUTCOME VARIABLES:	Age	Male(1) Female(0)	OBD(1) ONAD (0)	YES(1) NO(0)	YES (1) NO (0)
Suicidal Behavior	OR; 95% CI	OR; 95% CI	OR; 95% CI	OR; 95% CI	OR; 95% CI
Model chi-square: 24.591, p<.00 with df = 4	1.07; (.95 – 1.20)	.41; (.18 – .91)*	1.12; (.48 - 2.57)	5.67; (2.37 – 13.55)**	
Nagelkerk R-square = .222					
Regular Smoking					
Model chi-square: 11.112, p<.05 with df =4	1.11 (1.00 - 1.23)*	.85; (.42 – 1.75)	1.60 (.70 – 3.33)	1.98 (.87 – 4.52)	
Nagelkerk R-square = .1.01					
Sexual Risk Behavior					
Model chi-square: 49.532, p<.00 with df = 5	1.32 (1.17 - 1.48)**	.80 (.35 – 1.82)	2.32 (1.03 – 5.24)*	1.00 (.39 – 2.57)	13.80 (3.80 – 50.04)**
Nagelkerk R-square = .379					
Anti-Social Behavior					
Model chi-square: 23.651, p<.00 with df = 4	1.16 (1.05 - 1.30)**	4.22 (1.95 - 9.15)**	1.26 (.61 – 2.64)	1.02 (.42 - 2.49)	
Nagelkerk R-square = .201					

*p≤0.05, ***p≤0.01.

OR = odds ratio, df = degrees of freedom,

CI = confidence interval

Romantic Rel. = romantic relationship

CHAPTER 3. TRANSITION TO STUDY 2, MANUSCRIPT 2

3.1 Consequences of SRBs

It is clear that SRBs pose a significant threat to adolescent mental and physical health (Irwin, 1989; Irwin & Millstein, 1986). Indeed, these behaviors have shown strikingly high associations with adolescent morbidity and mortality rates. Traditionally, SRBs have been operationalized as initiating sexual activity before the age of 16 (i.e. Bricker, Stallings, Corley, Wadsworth, Bryan, Timberlake et al., 2006; Donahue, D'Onofrio, Lichenstein, & Langstrom, 2013; Dunne, Martin, Statham, Slutske, Dunwiddie, Bucholz, et al., 1997; Harden & Mendle, 2011; Paul, Fitzjohn, Herbison, & Dickson, 2000) and infrequent use of condoms (i.e. Caminis, Henrich, Ruchkin, Schwab-Stone, & Martin, 2007; Kosunen, Kaltiala,-Heino, Rimpelas, & Laippala, 2003; McNair, Carter, & Williams, 1998). It has been suggested that these behaviors reflect a deficit in emotion regulation and self-regulatory capabilities (Harden, 2012; Tull, Weiss, Adams, & Gratz, 2012) and that they are associated with impulsive tendencies. For example, SRBs co-occur with stress-related substance use (Tubman, Windle, & Windle, 1996), antisocial behavior (Capaldi, Crosby, & Stoolmiller, 1996; Harden & Mendle, 2011; Hasking, Sheirer, & Abdallah, 2011; Tubman et al., 1996), and a history of suicide attempts (Houck, Hadley, Lescano et al., 2008). Furthermore, there is indication that those who initiate sexual activity late, as opposed to early, report higher satisfaction in adult romantic relationships (Harden, 2012), suggesting that early sexual activity may further relate to deficits in the development of interpersonal skills. For these reasons, it is not surprising that SRBs have been associated cross-sectionally (Bachanas, Morris, Lewis-Gess, et al., 2002; Brooks, Harris, Thrall, & Woods, 2002; Kessler, Berglund, Foster,

Saunders, Stang, & Walters, 1997; Hipwell, Stepp, Keenan, Chung, & Loeber, 2011; Kosunen, Kaltiala-Heino, Rimpelas, & Laippala, 2003; Mazzaferro, Murray, Ness, Bass, Tyus, & Cook, 2006; Rubin, Gold, & Primack, 2009) and longitudinally (Brown, Tolou-Shams, Lesceno, et al.,2006; DiClemente, Wingood, Crosby et al., 2001; Hallfors, Waller, Bauer, Ford, & Halpern, 2005; Lehrer, Shrie, Gortmaker, & Buka, 2006) with adolescent depressive symptoms, with some evidence that this association is stronger among adolescents than young adults (Mazzaferro et al., 2006). Despite the impact of such behaviors, very little research has been conducted on the frequency of SRBs in high-risk populations. It is of interest to place these behaviors in a broader developmental context so as to understand the nature of their occurrence in our sample.

3.2 SRBs as an extension of externalizing problems

As previously mentioned, a prominent theory with regards to SRBs is that they are part of a larger set of problem behaviors, characterized by unconventionality, in youth with a history of externalizing problems (Donovan, Jessor, & Costa, 1991; Jessor & Jessor, 1977). Indeed, the literature appears to support that these behaviors stem from externalizing and, to a lesser extent, internalizing behavior problems seen in childhood (i.e. Caminis et al., 2007; Donengen et al., 2003; Siedenbruner, Zimmer-Gembeck, & Egeland, 2007). For example, adolescents with a history of conduct disorder tend to have earlier age of first intercourse (Emery, Waldron, Kitzmann, & Aaron, 1999; Woodward & Fergusson, 1999) and SRBs, particularly early initiation have been consistently associated with deviant or antisocial behavior in adolescence (Little & Rankin, 2001; Costa, Jessor, Donovan, & Fortenberry, 1995; Whitbeck, Yoder, Hoyt, & Conger, 1999). The relationship between externalizing behaviors and SRBs is suggested to be related to

traits such as impulsivity and inattention. These traits may interfere with an individual's ability to set limits, engage in self-control, and may also inhibit decision-making (Crockett, Raffaelli, & Shen, 2006; McLeod & Knight, 2010; Zimmer-Gembeck & Helfand, 2008). Conversely, there is also a suggestion that those who exhibit internalizing problems may engage in SRBs either because of low self-efficacy leading to low assertiveness and difficulty negotiating condom use (Donenberg et al., 2003) or as an attempt to counteract negative self image (Donovan & Jessor, 1985; Jessor, van den Bos, Vanderryn, Costa, & Turbin, 1995; Schofield, Bierman, Heinrichs, Nix, & the Conduct Problems Prevention Research Group, 2008; Whitbeck, Yoder, Hoyt, & Conger, 1999). However, some studies have found no link between SRBs and internalizing behavior problems (Donenberg et al., 2001; 2003; MacLeod & Knight, 2003), or have found internalizing problems to protect against adolescent sexual involvement (Tubman, Windle, & Windle, 1996). From the existent literature it would appear more likely that SRBs are an extension of aggressive or antisocial tendencies. Further longitudinal examinations of the relationship between early behavior problems and the subsequent development of SRBs would help to elucidate this claim.

3.3 The role of the family in the development of SRBs

There is some evidence that SRBs are influenced by family factors. Data from twin studies suggest an important role of shared family environment in the development of SRBs (Bricker et al., 2006; Donahue, D' Onofrio, Lichenstein, & Langstrom, 2013; Dunne et al., 1997; Guo & Tong, 2006; Mustanski, Viken, Kaprio, Winter, & Rose, 2007; Rodgers, Rowe, & Buster, 1999), however, it remains unclear as to what specific family environment factors contribute to the development of SRBs. Parent variables, such as low

parental monitoring (Boislard & Poulin, 2011; Li, Stanton, & Feigelman, 2000; Parkes, Henderson, Wight, & Nixon, 2011; Rose et al., 2005), as well low parent-child connectedness, less family cohesion, less overall expressiveness, and high levels of family conflict (Paul et al., 2000), trauma and/or maltreatment (Jaffee et al., 2004; Stein, Lang, Taylor, Vernon, & Livesley, 2002) have been shown as contributors to adolescent SRBs. However, the evidence of parents' influences on adolescent sexual risk behavior remains inconclusive, with some studies showing no relationship after controlling for potential confounds (Paul et al., 2000). To our knowledge, only one study has assessed parental contributions to SRBs in high-risk populations. Hadley, Hunter, Tolou-Shams, et al. (2012) showed that psychopathology in mothers predicted recent intercourse in their adolescent offspring, and that this relationship was mediated by low parental monitoring. However, many studies have examined parental influences concurrent to adolescent behavior (see Guilamo-Ramos, Bouris, Lee, et al., 2012 for review) making it difficult to ascertain the contribution of early parent-child interactions to the subsequent development of SRBs. . In general, hostile parent traits, such as hostile parenting behavior have been shown to predict children's' aggressive or antisocial behavior (Brook, Whiteman, & Zheng, 2002; Conger, Neppl, Kim, & Scaramella, 2003;Thornberry, Freeman-Gallant, Lizotte et al., 2003), however the link between parent traits specific to SRBs warrants further investigation.

3.4 Rationale for Study 2

Repetti and colleagues have proposed a model to explain influence of early family environment on problem behavior in at-risk offspring (Repetti, Taylor, & Seeman, 2002; Taylor, Lerner, Sage, Lehman, & Seeman, 2004). According to the model "risky

families", characterized by neglectful parenting or conflicts within the family, can have profound effects on infants' developing emotional processing, social skills and biological stress systems. During childhood, at-risk children fail to learn appropriate self- regulatory skills. This deficit in self-regulation impedes the development of social-emotional skills and adaptive coping strategies in response to stress. Risky behaviors (including SRBs) can be seen as a subsequent consequence of such deficits. During adolescence and adulthood, these behaviors act as risk factors for the development of mental and physical health problems. Based on this model and research in high-risk offspring, the second study focused on the putative link between parental neuroticism (a proposed contributor to "risky" family environments), childhood behavior problems and the subsequent development of SRBs in the OBD. A prospective longitudinal design was used to place SRBs within a context of parent traits and child problem behavior observed 10 years prior.

CHAPTER 4. STUDY 2, MANUSCRIPT 2: SEXUAL RISK BEHAVIORS IN THE ADOLESCENT OFFSPRING OF PARENTS WITH BIPOLAR DISORDER: ASSOCIATIONS WITH PARENTS' PERSONALITY AND EXTERNALIZING BEHAVIOR IN CHILDHOOD

4.1 INTRODUCTION

There is increasing evidence that childhood problem behaviors play an important role in the development of mental disorders among the offspring of parents with bipolar disorder (OBD; Duffy et al., 2007; Klimes-Dougan, Long, Lee, Ronsaville, Gold, & Martinez, 2010). Childhood behavior problems show both homotypic and heterotypic continuity over time (Broidy et al., 2003; Caspi, Moffitt, Newman, & Silva, 1996; Goodwin et al., 2004; Ostiguy, Ellenbogen, & Hodgins, 2012; Shiner, Masten, & Roberts, 2003). Investigations of the nature of such continuity in high-risk populations contributes to delineating risk pathways and prodromal features. Further, problem behaviors generate stress and increase exposure to suboptimal environments (Windle, 1994; Udry, Kovenock, Morris, & van den Berg, 1995) to which the OBD may be particularly sensitive.

Preschool aged OBD show elevated rates of internalizing problems including emotional dysregulation and somatic complaints (Maoz, Goldstein, Axelson, et al, 2013). They also exhibit heightened physiological responses to mild stressors (Zahn, Nurnberger, & Berrettini, 1989; Zahn, Nurnberger, Berrettini, & Robinson, 1991), biological sensitivity to stress in the natural environment (Ostiguy, Ellenbogen, Walker, Walker, & Hodgins, 2011), and attentional biases to emotional information (Gotlib, Traill, Montoya, Joormann, & Chang, 2005). These findings point to heightened sensitivity to the environment among the OBD, perhaps reflecting vulnerability. Notably,

there is evidence of the homotypic continuity of internalizing problems in the OBD (Ostiguy et al.,2012). Among OBD, the link between childhood internalizing problems and later symptoms of affective disorder is consistent with a clinical staging model (see Duffy, Alda, Hajek et al., 2010), that proposes the onset of non-mood disorders (i.e. anxiety, sleep disorders, learning disabilities) in childhood, followed in time by minor mood disturbance, depression and then mania. Several studies of the OBD support parts of this model (Duffy et al., 2007; Duffy et al., 2010; Duffy, Horrocks, Doucette et al., 2013; Goldstein, Shamseddeen, Axelson et al., 2010; Shaw, Gilliom, Ingoldsby, & Nagin, 2003). For example, in a prospective, longitudinal investigation of OBD and offspring of parents with no mental disorder (ONMD), we found evidence of continuity such that both internalizing and externalizing problems in childhood predicted deficits in offspring interpersonal functioning 10 years later (Ostiguy et al., 2012).

Some studies (Ellenbogen, Linnen, Santo et al., 2013; Diler, Birmaher, Axelson et al., 2011; Maoz, Goldstein, Axelson et al., 2014), but not all (Anderson & Hammen, 1993) have reported that externalizing problems are more prevalent among the OBD than ONMD. As early as toddlerhood, OBD have been distinguished from offspring of parents with other forms of psychopathology as displaying more behavioral disinhibition, novelty seeking and impulsivity (Hirschfield-Becker, Beiderman, Calltharp, Rosenbaum, Faraone, & Rosenbaum, 2003; Hirschfield-Becker, Beiderman, Henin, et al., 2006). In late childhood and adolescence, OBD display higher levels of sensation seeking (Nurnberger, Hamovit, Hibbs et al., 1988) and impaired executive functioning (Klimes-Dougan, Ronsaville, Wiggs, & Martinez, 2006; Meyer, Carlson, Wiggs et al., 2006). Externalizing problems among the OBD have been associated with the development of

mood disorders (Duffy et al, 2010), a severe course of mood disorder, and psychotic symptoms (Carlson & Weintraub, 1993; Egeland, Shaw, Endicott et al., 2003; Kilmes-Dougan, Long, Lee et al., 2010).

Some evidence suggests that childhood externalizing problems persist and diversify in adolescence among the OBD. We recently conducted a comprehensive assessment of personality and non-psychiatric risk factors, including self-reports of antisocial behavior, among the OBD and ONMD in late adolescence and early adulthood (Nijjar, Ellenbogen, & Hodgins, in press). The OBD reported engaging in significantly higher rates of sexual risk behaviors (SRBs), including early sexual initiation, frequent unprotected sex, and/or unplanned pregnancies (as indexed by abortions), than ONMD. Importantly, SRBs were independent of having developed an affective disorder, suggesting that they represent an additional psychosocial negative outcome in need of further study. Furthermore, the presence of SRBs appeared to represent a distinct form of risk behavior in the OBD, as they did not show higher rates of substance use disorders, smoking, criminality, self-injury, or suicidality than ONMD, although suicidality was elevated among the OBD who had developed an affective disorder. To date, most research on OBD has focused on mental disorders (i.e. Birmaher , Axelson, Goldstein, et al., 2010; Mesman et al., 2012), and has not assessed externalizing problems (with the exception of substance use disorders).

To the best of our knowledge, this is the first study to explore SRBs among OBD. In the general population, SRBs increase in prevalence during adolescence, co-occur with delinquent and anti-social behaviors (Capaldi, Crosby, & Stoolmiller, 1996; Costa, Jessor, Donovan, & Fortenberry, 1995; Harden & Mendle, 2011; Hasking, Sheirer, &

Abdallah, 2011; Little & Rankin, 2001; Tubman, Windle, & Windle, 1996; Whitbeck, Yoder, Hoyt, & Conger, 1999), and are preceded by externalizing behaviors in childhood (Capaldi, Crosby, & Stoolmiller, 1996; Costa, Jessor, Donovan, & Fortenberry, 1995; Harden & Mendle, 2011; Little & Rankin, 2001; Tubman et al., 1996; Whitbeck, Yoder, Hoyt, & Conger, 1999). Externalizing problems are associated with poor decision-making and self-regulatory capabilities (Harden, 2012; Tull, Weiss, Adams, & Gratz, 2012), trait impulsivity and unconventionality (Moffitt, Caspi, Dickson, Silva, & Stanton, 1996). Moreover, it has been suggested that SRBs are form of aggressive behavior that is seen in higher rates among females rather than males (Serbin & Karp, 2004). However, we did not find evidence for sex differences in SRBs in our previous cross-sectional study (Nijjar et al., in press).

SRBs are influenced by factors within the family environment. For example, low parental support, monitoring and control have been associated with SRBs (Capaldi, Stoolmiller, Clark, & Owen, 2002; Marchand & Smolkowksi, 2013; Metzler et al., 1994; Price & Hyde, 2009), as have low maternal attachment (Udell, Sandfort, Reitz, Bos, & Dekovic, 2010) and high levels of family conflict (Ary et al., 1999). Poor maternal mental health can impact the initiation of sexual activity in offspring, due in part to inadequate monitoring (Hadley, Hunter, Toulou-Shams et al., 2011). Thus, SRBs are associated with parental and family risk factors, many of which characterize parents with BD (i.e. Calam et al., 2012; Chang, Blasey, Ketter, & Steiner, 2001).

Parents' personality may be particularly important in understanding parenting practices, the home environment, and outcomes among offspring (Ellenbogen, Ostiguy, & Hodgins, 2010). We have recently postulated a model of intergenerational risk

transmission whereby OBD whose parents exhibit high trait neuroticism, not only inherit a tendency to overreact to stress but are also raised in unpredictable and chaotic home environments by parents who model ineffective coping skills and provide inadequate support and structure (Ostiguy, Ellenbogen, & Hodgins, 2012; Ellenbogen & Hodgins, 2004). In turn, these factors interact to predict deficits in emotional, behavioral, and physiological regulation among the children (Derryberry & Rothbart, 1997; Ellenbogen & Hodgins, 2009). As such, OBD are rendered vulnerable for maladaptive development not only through genes that are associated with affective disorders but also through exposure to family environments that enhance this genetic vulnerability. Moreover, as they grow up, genetically vulnerable offspring may seek out environments that are consistent with their own inability to cope with daily life and stress (Rutter, 2007; Rutter, Moffitt, & Caspi, 2006).

Recently, we demonstrated support for this model (Ostiguy, Ellenbogen, & Hodgins, 2012). In our longitudinal study, high levels of neuroticism in parents were associated with offspring internalizing and externalizing problems in childhood and they predicted deficits in offspring interpersonal functioning 10 years later (Ostiguy et al.,2012). Low agreeableness in parents also predicted poor interpersonal functioning in their offspring 10 years later, and this association was mediated by externalizing problems in offspring during middle childhood (Ostiguy et al., 2012). Moreover, the association between parents' neuroticism and child internalizing problems was stronger among the OBD than the ONMD, suggesting that the risk of developing internalizing problems was stronger for offspring who had a parent with both BD and high neuroticism.

The goal of the present study was to determine whether parents' personality traits promote externalizing problems in childhood that persist and manifest as SRBs in adolescence and young adulthood. Based on our previous findings (Ostiguy et al., 2012), we hypothesized that parents' neuroticism would predict SRBs among their offspring. Further, based on our finding that parents' neuroticism was associated with offspring externalizing problems in childhood and the large body of evidence showing that childhood externalizing problems are antecedents of SRBs (i.e. Caminis et al., 2007; Donengen et al., 2003), we hypothesized that the association between parents' neuroticism and offspring SRBs in late adolescence and early adulthood would be mediated by parent-rated childhood externalizing problems. We explored whether the five facets of neuroticism and other personality traits of the parents were associated with offspring SRBs and whether any associations were mediated by offspring externalizing problems in childhood. We expected that mediation of associations between parents' personality traits and offspring SRBs would be more robust in the OBD than the ONMD. As would be expected, our previous study found that antisocial behavior was more common among males than females (Nijjar et al., in press). Therefore we determined whether sex of the offspring moderated the relationship between childhood behavioral problems and SRBs. The analyses predicting SRBs controlled for lifetime affective disorder diagnoses in an effort to further understand the continuity of risk behavior. All analyses were run a second time using teacher-rated childhood externalizing ratings in order to examine externalizing behaviors that were seen in both inside and outside of the home. Analyses were also re-run to determine whether childhood internalizing problems contributed to subsequent SRBs.

4.2 METHOD

Participants

The sample included 102 offspring (49 females [48.0%] and 53 males [51.9%]) from 72 families. Families were participants in a longitudinal prospective study comparing the development of OBD and ONMD. Parents with BD and their children were recruited form psychiatric outpatient clinics and from patient advocacy and support groups. Parents with no mental disorder were recruited from the same neighborhoods as families with BD, through physician's office and community organizations. At baseline, the inclusion criteria for the study were a) adults raising at least one biological child between the ages of 4 -14 years, b) fluency in English or French, c) being raised and educated in Canada. Families were excluded from the study if either the parent or child had a chronic physical disease, or handicap and/or an IQ below 90. Of the original sample, there was an attrition rate of 18 % among OBD and 17% among ONMD. Offspring who did not participate in the follow-up did not differ from those who did on ratings of childhood behavior problems or IQ. At the initial assessment, parents completed a diagnostic interview, using the Structured Clinical Interview for the DSM-III-R; Spitzer, Williams, Gibbon, & First, 1992). On average, parents with BD reported disorder onset 7.85 years (SD = 8.65) before the birth of the child included in the study. The comparison group parented presented no current Axis I conditions, five met criteria for a past drug use or anxiety disorder (detailed information on the original sample can be found in Ellenbogen & Hodgins, 2004).

In the present study, offspring ranged in age from 14 -25 years (M = 19.07; SD = 2.90). Fifty-two offspring (51.0%) from 41 families had a parent with BD and 50

offspring (49.0 %) from 31 families had a parent with no mental disorder. Of the 41 families with BD, 19 had mothers who were affected and 22 had father with BD. In addition, 13 families had one parent with BD and one parent with major depression. Twenty-four offspring (16 OBD [30.7%]; 8 ONMD [16.0%) met DSM-IV (American Psychiatric Association, 1994) criteria for a current diagnosis including two mood disorders (2 OBD [3.8%]; 0 ONMD), 16 anxiety disorders (9 OBD [17.3%], 7 ONMD [14.0%]), substance-related disorders (4 OBD [7.7%], 2 ONMD [4.0%]), and 3 other diagnoses (1 OBD [1.9%] with hypochondriasis, 1 OBD [1.9%] with ADHD, and 1 ONMD [1.9%] with Tourette syndrome).

Measures

Time 1 (1995-1997; children aged 4-12 years old.

Revised NEO Personality Inventory (NEO-PI-R)

This 240 item self-report questionnaire assesses five personality traits including neuroticism (Costa & McCrae, 1992). Given our previous findings showing strong associations between parents' level of neuroticism, the home environment, and offspring childhood behaviors, we also examined the five facets of the neuroticism scale: anxiety, angry hostility, depression, self-consciousness, and impulsiveness. Excellent psychometric properties have been demonstrated for this measure, including high internal consistency, with coefficients ranging from .89 to .95, and temporal stability over 6 years (Costa, Herbst, McCrae, & Siegle; 2000; Costa & McCrae, 1992; Rolland, Parker, & Stumpf, 1998), as well as convergent and discriminant validity (Costa & McCrae, 1992). Similar psychometric properties have been demonstrated with the French translation (Rolland et al., 1998). Parent personality data was available for two parents for ninety-

nine offspring. For these offspring, an average score was computed across both parents on trait and facet scores; 6 offspring had personality data from only one parent.

Child Behavior Checklist (CBCL; Achenbach, 1991)

Information on internalizing and externalizing behaviors in offspring were obtained through the Parent Report Form (PRF) of the Child Behavior Checklist (CBCL). Good reliability and validity have been demonstrated for the PRF (Achenbach & Rescorla, 2001; Barkley, 1998). Furthermore, concurrent validity has been established for the CBCL and other parent-reported behavior scales (Barkley, 1988). For 95 offspring, a mean score was computed from two parents; seven offspring had ratings from one parent only. Teacher ratings of the CBCL teacher version were available for 70 offspring.

Time 2 (2006-2008; children aged 14-25 years old)

Diagnostic Interviews

The Structured Clinical Interview for DSM-IV (SCID-I; First, Gibbon, Spitzer, & Williams, 2002) was administered to offspring aged 19-years or older to assess mental disorders. The Kiddie-Schedule for Affective Disorders and Schizophrenia- Present and Lifetime version (K-SADS-PL; Kaufman, Birmaher, & Brent, Rao, Flynn, Moreci, et al., 1997) was used to assess mental health in offspring aged 18 years and younger. Both interviews have been shown to be highly reliable and valid diagnostic instruments (i.e. Ramirez-Basco, Bostic, Davies, Rush, Witte, Hendrickse et al., 2000; Kaufman, Schweder, Hilsenroth, & Segal, 2004). Interviews were conducted by experienced clinicians who were specifically trained and supervised in the use of the official English and French versions of the SCID or K-SADs.

High-Risk Sexual Behavior

An in-house structured interview was used to assess SRB defined as unprotected sex, abortions, and sexual intercourse before the age of 16. The latter item was based on research showing that sexual intercourse before the age of 16 is linked to maladaptive developmental outcomes (Spriggs & Halpern, 2008a; Spriggs & Halpern, 2008b; Darroch, Frost, & Singh, 2001; Madkour, Farhat, Halpern, Godeau, & Gabhainn, 2010).

Procedure

Time 1: Following recruitment and telephone screening, parents were interviewed, in the laboratory or in their homes, using the SCID-I, and they completed questionnaires including the NEO-PI-R and the CBCL-PRF (for a full list of measures obtained see Ellenbogen & Hodgins, 2004). Interviews and questionnaires were completed when the parents with BD were euthymic. Spouses were subsequently contacted to complete the same interview and battery of questionnaires, and offspring, aged 4-14 years old were assessed using a diagnostic interview (not included in the present study; see Ellenbogen & Hodgins, 2004).

Time 2: The offspring were contacted for the follow up assessment when they reached late adolescence-early adulthood (N= 102, mean age = 19.07 years-old). In the laboratory, they underwent a diagnostic assessment and structured interview on SRBs and other risk behaviors by an experienced clinician or senior graduate student in clinical psychology. They also completed questionnaires and underwent a computerized assessment of emotional information processing, and in the following days collected saliva samples for cortisol extraction in their natural environment (not included in the present study). Participants were remunerated $ 150 CAN for taking part in the full data

collection. All procedures were approved by the Human Research Ethics Committee of Concordia University.

Data Analyses

Prior to testing hypotheses, data were screened for outliers, violations of normality, and the need for transformation. Comparisons of the OBD and ONMD on dependent and independent variables are provided in Table 1. The Pearson correlation coefficients for zero-order correlations among variables are displayed in Table 2.

Multiple mediation was used to assess whether externalizing and internalizing behavior problems in middle childhood mediated the relationship between parents' neuroticism and offspring SRBs 10 years later. The analysis was then repeated using teacher reports of child's externalizing and internalizing behavior problems. To test our mediation hypotheses, we used the bootstrapping method with bias-corrected confidence estimates (MacKinnon, Lockwood, & Williams, 2004; Preacher & Hayes, 2004). Bootstrapping is an increasingly preferred alternative to the Sobel test (Baron & Kenny, 1986) to assess mediation models in smaller samples (Lockwood & McKinnon, 1998; Preacher & Hayes, 2004; Shrout & Bolger, 2002). The analyses and bootstrapping estimates that follow are based on 5000 bootstrap samples and accelerated 95% confidence intervals. Age and current affective disorder diagnosis were entered as covariates in all analyses. Parents' level of education was used as a proxy for SES in this sample and was used also entered as a covariate. Mediation analyses compare direct effects (the strength of the association between the independent variable and dependent variable before the proposed mediators are entered into the equation), total effect (the strength of the association between independent variable and dependent variable once the

mediators are accounted for) and indirect effects (the strength of the mediating pathway). Current mediation analyses no longer require a prerequisite significant association between the independent variable and dependent variable if there is reason to believe that the indirect pathway is stronger than the direct association among variables (Collins, Graham, & Flaherty, 1998; MacKinnon, 2000; Rucker, Preacher, Tormala, & Petty, 2011). Therefore, indirect effects were tested even in the absence of direct effects. To determine whether the mediated relationship between parents' neuroticism, offspring externalizing problems in middle childhood, and offspring SRBs differed by risk status or sex, moderated mediation analyses were conducted. Analyses were computed using the MODMED macro (Version 2.0, Model 2; see http://www.afhayes.com/public/modmed.pdf).

4.3 RESULTS

Mediation analyses of the relationship between parents' neuroticism and high-risk sexual behavior in offspring

Parent-rated offspring externalizing and internalizing scores, assessed in middle childhood, were tested as potential mediators of the relationship between parents' personality and offspring SRBs. As shown in Figure 1, after controlling for age (b = .21, se = .09, p = .03), the presence of a current affective disorder (b = -1.66, se = 1.52, p = .28), and parents' education level (b = -.42; se = .41, p = .31), parents' neuroticism scores did not have a significant total effect on offspring SRBs (Figure 1-A; b= -.00, se = .03, p = .90), nor did neuroticism have a direct effect (Figure 1-B; b = -.05, se = .03, p = .11). There was a significant indirect effect of offspring externalizing problems on the relationship between parents' neuroticism scores and offspring SRBs (b = .05, SE = .02;

lower 95% CI = .02, upper 95% CI = .10). Specifically, high neuroticism in parents was positively associated with offspring externalizing behaviors in childhood, and offspring externalizing behaviors in childhood were positively associated with offspring SRBs a decade later. Offspring internalizing problems did not mediate the relationship between parents' neuroticism and subsequent SRBs among the offspring (b = .01, SE = .01; lower 95 % CI = -.03, upper 95 % CI = .04).

A second multiple mediation analysis was conducted in order to examine the mediation of parents' neuroticism and offspring SRBs by teacher-rated offspring externalizing and internalizing problems. Results were similar, but less significant, than those obtained with parents' ratings, perhaps due to the smaller sample of only 70 offspring. Parents' neuroticism scores did not have a significant total effect (Figure 2-A) on offspring SRBs nor did it have a direct effect (Figure 2-B). The mediation analysis examining the indirect effect of parents' neuroticism on SRBs through externalizing behaviors fell short of conventional statistical significance (b = .02, SE = .02, lower 95 % CI = -.0134, upper 95% CI = .1111; Figure 2-B). Offspring internalizing problems, did not mediate the relationship between parents' neuroticism and offspring SRBs (b = -.00, SE = .01, 95 % CI = -.0415-.0159; Figure 2-C).

Mediation Analyses with Facets of Neuroticism

Secondary exploratory analyses were conducted to determine whether the reported findings were being driven by a specific facet of neuroticism, particularly the impulsiveness facet. Thus, the mediation analyses described above were repeated using each facet of the neuroticism factor. The results of the analyses with each of the five facet

scores (anxiety, impulsivity, hostility, depression, self-consciousness) were comparable to those reported for neuroticism scores, suggesting that no one facet was responsible for the reported indirect effect of parents' neuroticism on subsequent SRBs among the offspring.

Mediation analyses of the relationship between other personality traits in parents and high risk sexual behavior in offspring

Similar multiple mediation analyses were undertaken to ascertain the contribution of other personality traits (openness to experience, conscientiousness, extraversion, and agreeableness) of the parents to offspring SRBs. Parents' agreeableness scores showed an indirect relationship with SRBs via childhood externalizing problems, but not via internalizing problems (95% CI = -.1057- -.0076), as did parents' extraversion scores (95% CI = -.1061 -.0068, see Table 3). Results suggest that low parental agreeableness and low parental extraversion predicted offspring SRBs indirectly via the offsprings' externalizing problems in childhood. Parents' openness to experience and conscientiousness scores showed no direct or indirect relationships to offspring SRBs.

Examining the moderation of the relationship between parents' personality and offspring SRBs by risk status and sex.

Two regression analyses were conducted to assess whether offspring risk status moderated the pathway between parents' neuroticism and offspring externalizing problems (see Table 4). Risk status (having a parent with BD) was a statistically significant moderator of the relationship between parents' neuroticism scores and

offspring externalizing problems. Specifically, the strength of the indirect relationship between parents' neuroticism and offspring externalizing problems was stronger for the OBD than ONMD. Risk status did not moderate the pathway between externalizing problems and SRBs.

Sex did not moderate the association between parents' neuroticism and offspring externalizing behaviors in childhood, nor the association between the offsprings externalizing behavior and later SRBs (see Table 4). Next, the above moderated mediation analyses with offspring risk status and sex were repeated using offspring internalizing problems as the mediator. None of these analyses yielded significant findings. The moderated mediation analyses above were repeated with parents' agreeableness and extraversion as predictors of externalizing problems and SRBs. No evidence of moderated mediation was found for pathways involving parents' agreeableness or extraversion.

4.3 DISCUSSION

The current prospective longitudinal study, comparing OBD and ONMD, examined the contribution of parents' personality factors to the prediction of SRBs among offspring in adolescence and early adulthood, and assessed whether this relationship was dependent on the presence of externalizing or internalizing problems among the offspring in middle childhood. Overall, no direct relationship between parents' personality and SRBs in their offspring was observed. Rather parents' high neuroticism, low agreeableness, and high extraversion indirectly predicted offspring SRBs via the offspring's externalizing problems in middle childhood. Moderated mediation analyses

confirmed that the relationship between parents' personality and offspring SRBs was more robust in the OBD than among the ONMD, at least for the pathway from parents' neuroticism to child externalizing problems. Importantly, results were similar using parent- and teacher-ratings of the offspring's behavior in middle childhood, although teacher ratings were not available for all offspring and results only reached trend levels. To our knowledge, this is the first study to assess the impact of parents' personality on the development of SRBs among the OBD, as they pass through puberty and transition to adulthood. The results identify one pathway of inter-generational risk transmission.

The association between parents' personality and offspring SRBs extends our past findings showing that parents' neuroticism predicted offspring interpersonal functioning during late adolescence and early adulthood mediated by offspring internalizing problems in childhood (Ostiguy et al., 2012). Thus, although overlap is likely, it appears that trajectories to interpersonal problems and SRBs are somewhat distinct, despite being associated with high negative emotionality in parents. The fact that externalizing problems, but not internalizing problems, predicted SRBs over a 10-year period is consistent with previous evidence that SRBs are linked to early externalizing problems in other populations (McLeod & Knight, 2010; Jones et al., 2012). It has been suggested that childhood externalizing problems persist and diversify in adolescence to include risky sexual practices, and reflect a broader behavioral syndrome characterized by unconventionality, deficits in self-regulation, and poor decision-making (Jessor & Jessor, 1977).

Consistent with our previous report (Ostiguy et al, 2012), the present study also found evidence of increased sensitivity to parents' personality among the OBD relative to

the ONMD. Offspring risk status moderated the association between neuroticism in parents and childhood externalizing behavior problems, but not the association between childhood externalizing problems and subsequent SRBs. In other words, offspring of parents who had both BD and high neuroticism were more likely than offspring of parents with high neuroticism alone to develop externalizing problems. However, once externalizing problems developed, both the OBD and ONMD were equally likely to develop SRBs. These results are in line with studies documenting higher rates of externalizing problems in the OBD than in comparison samples (Gilles, Delbello, Stanford, & Strakowski, 2007; Klimes-Dougan, Long, Lee, Ronsaville, Gold, & Martinez, 2010; Linnen, aan het Rot, Ellenbogen, & Young, 2009). Importantly, the present findings provide further evidence that the OBD display an increased sensitivity, indexed by elevated rates of both internalizing and externalizing problems in childhood, to their parents' negative emotionality. In a previous study, relationships between cortisol levels and interpersonal stress in the natural environment were stronger in the OBD than the ONMD suggesting that the OBD may exhibit a heightened biological sensitivity to naturalistic stress (Ostiguy et al., 2011). Taken together, the results suggest that OBD may exhibit a more general sensitivity to environmental stress, and having a highly neurotic parent is stressful.

The trait of neuroticism in parents may have a negative impact on children for a number of reasons, including more expressed negative emotion in the household and compromised parenting practices (Ellenbogen & Hodgins, 2004). Neuroticism is a trait defined by negative emotionality, especially in situations involving threat, frustration or loss (Costa & McRae, 1992a; Eysenck & Eysenck, 1975) and signals a less adaptive

response to stress (Bolger & Zuckerman, 1995; Connor-Smith & Flachsbart, 2007). Individuals high on this trait readily experience emotions such as anger, sadness, guilt, and irritability, and also struggle with social and occupational problems, generate more stress in their day-to-day lives, and are less efficient at coping with stressors (Belsky & Barends, 2002; DeLongis & Holtzman, 2005; Ellenbogen & Hodgins, 2004; Oppenheimer, Hankin, Jenness, Young, & Smolen, 2013; Watson, Gamez, & Simms, 2005). Furthermore, high neuroticism in parents has been associated with a range of non-optimal parenting practices including low warmth, low autonomy support, and ineffective behavioral control (Prinzie, Stams, Dekovic et al., 2009), as well as a less organized and consistent parenting style (Ellenbogen & Hodgins, 2004). It is important to note that children's defiance is a considerable source of distress for parents (Rothbart & Bates, 2006). As such, high levels of neuroticism may compound poor parenting practices in rendering the parent less able to cope with children displaying externalizing problems. Such problematic parent-child interactions may in turn perpetuate further maladaptive parenting practices and negative outcomes in offspring. Unfortunately, the effects of parents' neuroticism on child outcomes, despite evidence of its deleterious effects, continue to be neglected as a potential risk factor for children (Ellenbogen, Ostiguy, & Hodgins, 2010; Kochanska, Clark, & Goldman, 1997).

Parents' traits of conscientiousness and openness to experience were not related to adolescent SRBs, while agreeableness and extraversion both showed a negative indirect association with offspring SRBs via offspring externalizing problems in childhood. Low agreeableness has been associated with less responsive parenting (Clark, Kochanska, & Ready, 2000; Kochanska, Clark, & Goldman, 1997), as well as the more frequent use of

coercion, forceful insistence, and a critical interaction style (Kochanska, Kim, & Nordling, 2012). Furthermore, a review of the literature has shown that of the Big Five personality traits, neuroticism and agreeableness were uniquely related to the parenting dimension of autonomy support-coercion (Prinzie et al., 2009). It has been proposed that parents with high levels of neuroticism and low levels of agreeableness are more likely to attribute negative intentions to children's non-compliant behavior, leading to the use of harsh punishment and coercive parenting (Bugental & Shummen, 1984; Prinzie et al., 2009). High neuroticism and low agreeableness also contribute to trait anger (Matrin, Watson, & Wan, 2000), which may account for hostile exchanges between parents and children. High extraversion has been linked to positive parenting practices including more dyadic exchange and symbolic play, parents' feelings of competence (Bornstein, Hahn, & Haynes, 2011), as well as warm and structured parenting (Belsky, Crnic, & Woodworth, 1995; Clark et al., 2000; Prinzie et al., 2009). Thus parents' personality traits of high neuroticism, and low agreeableness and extraversion are associated with non-optimal parenting practices such as low support and low structure, that in turn are associated with externalizing problems among their children. Results of the present study indicated that these externalizing problems persist and diversify as offspring transition to adulthood.

The association of parents' personality with offspring SRBs in late adolescence and early adulthood that was mediated by offspring externalizing problems in childhood may be explained, at least in part, by gene-environment interactions. Several of the genetic polymorphisms associated with externalizing problems have been found to confer sensitivity to the environment such that exposure to positive environmental factors leads

to better than average outcomes while exposure to negative factors leads to negative outcomes (i.e. Belsky & Beaver, 2011; Belsky, Jonassaint, Pluess et al., 2009a; Belsky & Pluess, 2009b). For example, in a study of three geneotypes, brain-derived neurotrophic factor (BDNF) gene (Val66Met), the serotonin transporter gene linked polymorphic region (5-HTTLPR), the monoamine oxidase A gene (MAOA-uVNTR), none was directly related to teenage delinquency. However, the high activity variants, that is BDNF Val, 5HTTLPR LL, MAOA-uVNTR LL (girls) and L (boys) as compared to the low activity variants, BDNF Val/Met, 5HTTLPR S/LS, MAOA-uVNTR S/SS/LS), in interaction with family conflict and sexual abuse, were associated with the highest delinquency scores, while in interaction with a positive parent-child relationship these same genetic variants were associated with the lowest delinquency scores (Nilson, Comasco, Oreland et al., under review). Similarly, environmental factors modify the effects of genes on alcohol use disorder. Single nucleotide polymorphisms (SNPs) of adrenergic genes (rs60218 and rs521674 in ADRA2A) interacted with physical abuse in childhood to increase the probability of alcohol use disorder and interacted with a positive parent-child relationship to decrease the probability of alcohol use disorder (Hodgins, Rehn, Westerman et al., under review). Thus, if parents' neuroticism and low agreeableness and extraversion limit the quality of their relationship with their offspring, the offspring will remain vulnerable to the effects of genes conferring vulnerability for externalizing behaviors.

Another possible mechanism by which parents' personality traits may be linked to offspring SRBs is early pubertal timing. Stressors in the family environment, including increased negativity and coercion, are reported to lead to accelerated pubertal

development, fostering earlier initiation of intercourse, more promiscuity, and less stable pair bonds in offspring (Belsky, Steinberg & Draper, 1991), while greater parent-child warmth and cohesion forecasts later pubertal development in girls (Ellis & Essex, 2007; Ellis, McFayden-Ketchum, Dodge, Petit, & Bats, 1999; Graber, Brooks-Gunn, & Warren, 1995; Steinberg, 1988). Furthermore, harsh parenting and child maltreatment have been shown to predict early pubertal development in daughters (Belsky, Steinberg, Houts et al., 2007; Costello, Sung, Worthman, & Angold, 2007; Tither & Ellis, 2008). The association between low parental supportiveness and pubertal timing is specific to children who show a higher biological susceptibility to stress (Ellis, Shirtcliff, Boyce et al., 2011). Future studies could investigate whether pubertal timing in offspring is linked to personality traits of parents with BD, and whether in turn it promotes the persistence and diversification of externalizing problems through adolescence and into early adulthood.

SRBs have both short and long-term negative consequences for adolescents and young adults. For OBD who are at risk for major affective disorders the consequences may be more even more severe as SRBs increase stress both in the short term, for example, increased rates of sexually transmitted diseases or experiencing an abortion, and in the long term, for example, giving birth to a child at a young age. The results of the present study identify targets for preventing the development of SRBs among the OBD. Specifically, based on the results of this study, it would seem that the OBD would benefit from interventions that address externalizing behaviors in middle childhood. Furthermore, targeting trait neuroticism and agreeableness in parents may contribute to adaptive development in their offspring. Trait neuroticism may be amenable to a range of

interventions (Lahey, 2009; Ormel et al., 2013), including those designed to aid in stress management (Antoni, Cruess, Cruess et al., 2000; Hampel, Meier, & Kummel, 2008). Adults with BD who propose having children could be encouraged to complete parenting programs and randomized controlled trials could determine whether reductions in neuroticism and increased agreeableness and extraversion among parents with BD would improve family functioning and parenting practices and positively impact the development of their offspring. If these windows of opportunity for intervention are missed, parents with BD who have children presenting externalizing problems could be encouraged to complete parenting programs that have been shown to effectively reduce externalizing problems in offspring.

The strengths of this study are the unique sample of parents with BD and their children; the use of a prospective intergenerational, longitudinal design, diagnostic interviews conducted on all parents and offspring with high inter-rater reliability, and measures of offspring behavior from multiple informants. Several limitations that warrant consideration include the fact that the sample was small, and, as such, non-significant findings, especially regarding moderated mediation, should be interpreted with caution. Additionally, the limited sample size prevented investigation of maternal and paternal influences on adolescent SRBs that a recent meta-analysis suggests contribute uniquely to SRBs among offspring (Guilamo-Ramos, et al., 2012). The inclusion of siblings transgresses the independence of cases assumption. However, the findings were replicated in a sub-sample that included only one child per family, suggesting that the present results are not due to alpha inflation associated with the non-independent data. Another potential limitation in this study was that information on SRBs was obtained

through self-report and, given the sensitive nature of such questions, may have been under-reported. However, the "age at first intercourse" measure is a frequently used SRB research, and is believed to be less susceptible to reporter bias (Epstein, Bailey, Manhart et al., 2014; Zimmer-Gembeck & Helfand, 20008). Unfortunately, there are few objective measures in this area of research, and those that are used (i.e. pregnancy in adolescence) did not occur at a high frequency in the current sample.

To conclude, this is the first study, to our knowledge, to examine factors contributing to the development of SRBs among adolescents and young adults at presumed genetic risk for major affective disorders. Parents' high negative emotionality was associated with offspring SRBs via offspring externalizing problems in childhood. These associations were stronger among the OBD than the ONMD. Our previous findings showed that high levels of neuroticism in parents was associated with poor parenting, specifically a lack of support and structure, and with both externalizing and internalizing problems among offspring in middle childhood (Ellenbogen & Hodgins, 2009). In a recent report we showed that internalizing problems mediated the association of offspring interpersonal functioning by early adulthood (Ostiguy et al., 2012). The present study shows a pathway to SRBs through parents' high neuroticism and low agreeableness and extraversion and childhood externalizing problems. Taking together these results highlight the importance of reducing neuroticism and increasing agreeableness and extraversion among adults with BD. Targeted interventions may improve their own psychosocial functioning, including parenting practices, and prevent the development of problem behavior among their offspring.

Table 1. Descriptive statistics for dependent and independent variables

	OBD	ONMD	Total	F
N	52	50	102	
Sex of offspring (female: male)	23:29	26:24	49:53	.46
	M ± SD	*M ± SD*	*M ± SD*	
		Time 1 (1995-1997)		
Offspring Age	8.50 ± 2.44	7.49 ± 2.30	8.01 ± 2.42	4.75*
Offspring CBCL t scores				
Externalizing	53.11 ± 11.46	44.18 ± 9.08	48.78 ± 11.26	19.40**
Internalizing	53.16 ± 9.74	47.02 ± 7.58	50.15 ± 9.24	12.76**
Parents' Neuroticism t-score	53.31 ± 7.85	45.65 ± 60.02	49.58 ± 7.97	30.92**
		Time 2 (2006-2008)		
Offspring Age	20.09±2.56	18.88±2.53	19.5±2.61	5.92*
	Freq(%)(N)	*Freq(%)(N)*	*Freq(%)(N)*	χ^2
High Risk Sexual Behaviour	68.0% (34)	54.0% (27)	60.0% (61)	1.37
Early Initiation	50.0% (26)	48.0 % (24)	49.0% (50)	.04
Frequent Unprotected Sex	44.2% (23)	32.0% (16)	38.2% (39)	.11
Abortion	7.4% (4)	5.9% (3)	6.9% (7)	1.62

Note: OBD, offspring of parents with bipolar disorder; ONMD, offspring of parents with no mental disorder; CBCL, Child Behaviour Checklist; * p<.05; **p<.01.

Table 2. Pearson correlation coefficients for dependent and independent variables

Variable	1	2	3	4	5	6
1) Parental Neuroticism	----					
2) Offspring Externalizing Problems in Childhood (parent report)	.509**	----				
3) Offspring Internalizing Problems in Childhood (parent report)	. 571**	.678**	----			
4) Offspring Externalizing Problems in Childhood (teacher report)	.346**	.612**	.234*	----		
5) Offspring Internalizing Problems in Childhood (teacher report)	.250*	.462**	.571**	.485**	----	
6) High-Risk Sexual Behaviour	-.004	.237*	.033	.121	-.058	----

* p<.05; ** p<.01.

Table 3. Standardized path coefficients for direct and indirect effects of parents' openness to experience, conscientiousness, extraversion, and agreeableness on offspring sexual risk behaviour

	β	SE	p	
Total effects				
Openness to Experience	-.02	.12	.56	
Conscientiousness	-.00	.04	.95	
Extraversion	-.00	.03	.94	
Agreeableness	.04	.04	.30	
Direct Effects				
Openness to Experience	.02	.03	.51	
Conscientiousness	.01	.04	.74	
Extraversion	.02	.04	.61	
Agreeableness	.07	.04	.07	
Indirect Effects (Mediation Tests)				
				95 % CI
Openness to Experience				
Parental trait → externalizing problems	-.02	.12	.86	-.0394, .0223
Externalizing problems → SRBs	.07	.03	.02	
Parental trait → internalizing problems	.05	.08	.66	-.0078, .0162
Internalizing problems → SRBs	.02	.03	.56	
Conscientiousness				
Parental trait → externalizing problems	-.19	.13	.15	-.0554, .0045
Externalizing problems → SRBs	.08	.03	.02	
Parental trait → internalizing problems	-.10	.09	.25	-.0256, .0090
internalizing problems → SRBs	.02	.04	.64	
Extraversion				
Parental trait → externalizing problems	-.32	.13	.01	-.0684, -.0030*
Externalizing problems → SRBs	.08	.03	.02	
Parental trait → internalizing problems	-.18	.09	.04	-.0296, .0166
internalizing problems → SRBs	.03	.04	.65	
Agreeableness				
Parental trait → externalizing problems	-.37	.13	.01	.0286, .0166*
Externalizing problems → SRBs	.09	.04	.01	
Parental trait → internalizing problems	-.21	.09	.02	-.0345, .0162
internalizing problems → SRBs	.03	.05	.47	

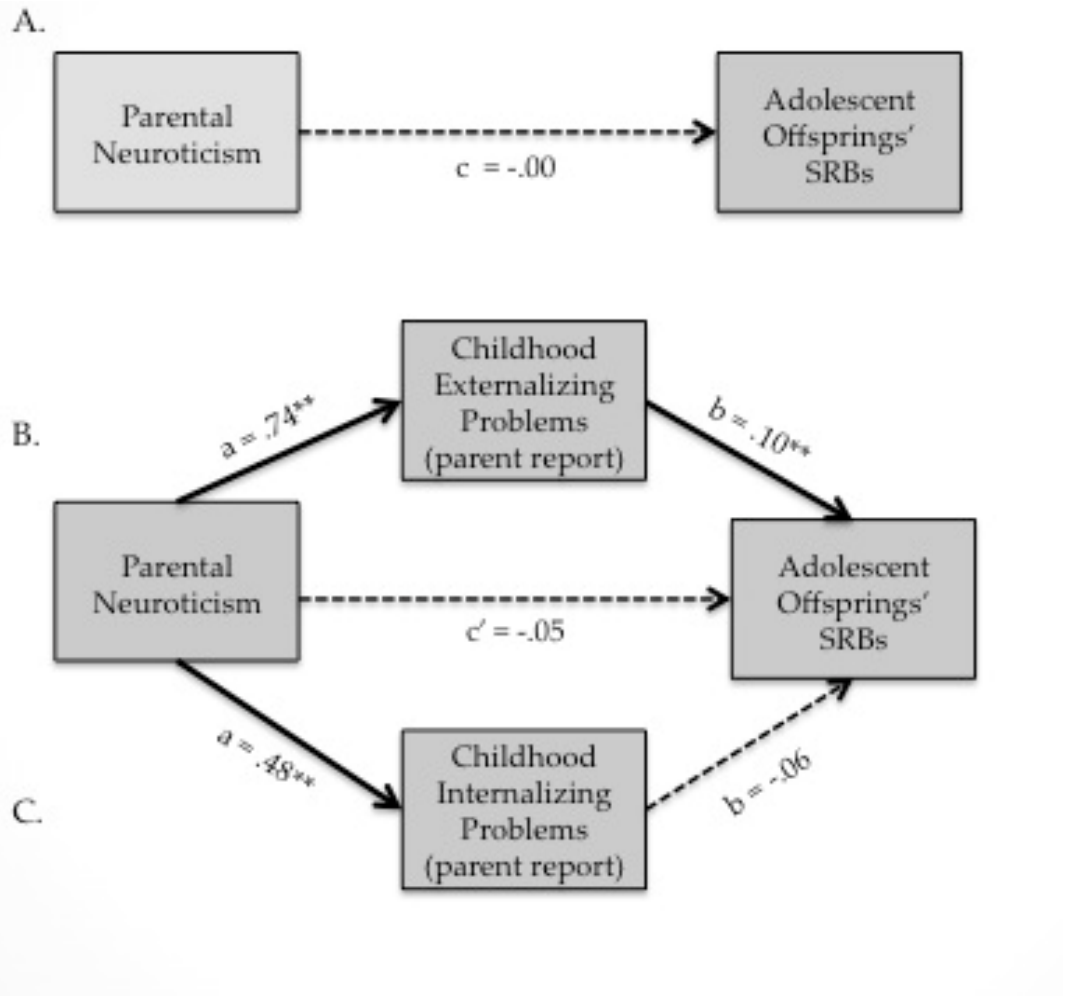
Note: * $p<.05$; SRB sexual risk behavior.

Table 4. Tests of moderated mediation for the relationship between parents' neuroticism, externalizing problems in childhood, and offspring sexual risk behaviours

Indirect Effects	b	SE	95% CI
Parents' neuroticism to offspring externalizing problems			
Via Risk status	-.14	.07	.0019 - .2796*
Via Sex	.35	.25	-.1362 - .8422
Offspring externalizing problems to SRBs			
Via Risk status	-.02	.05	-.1057 - .0759
Via Sex	.04	.04	-.0492 - .1243

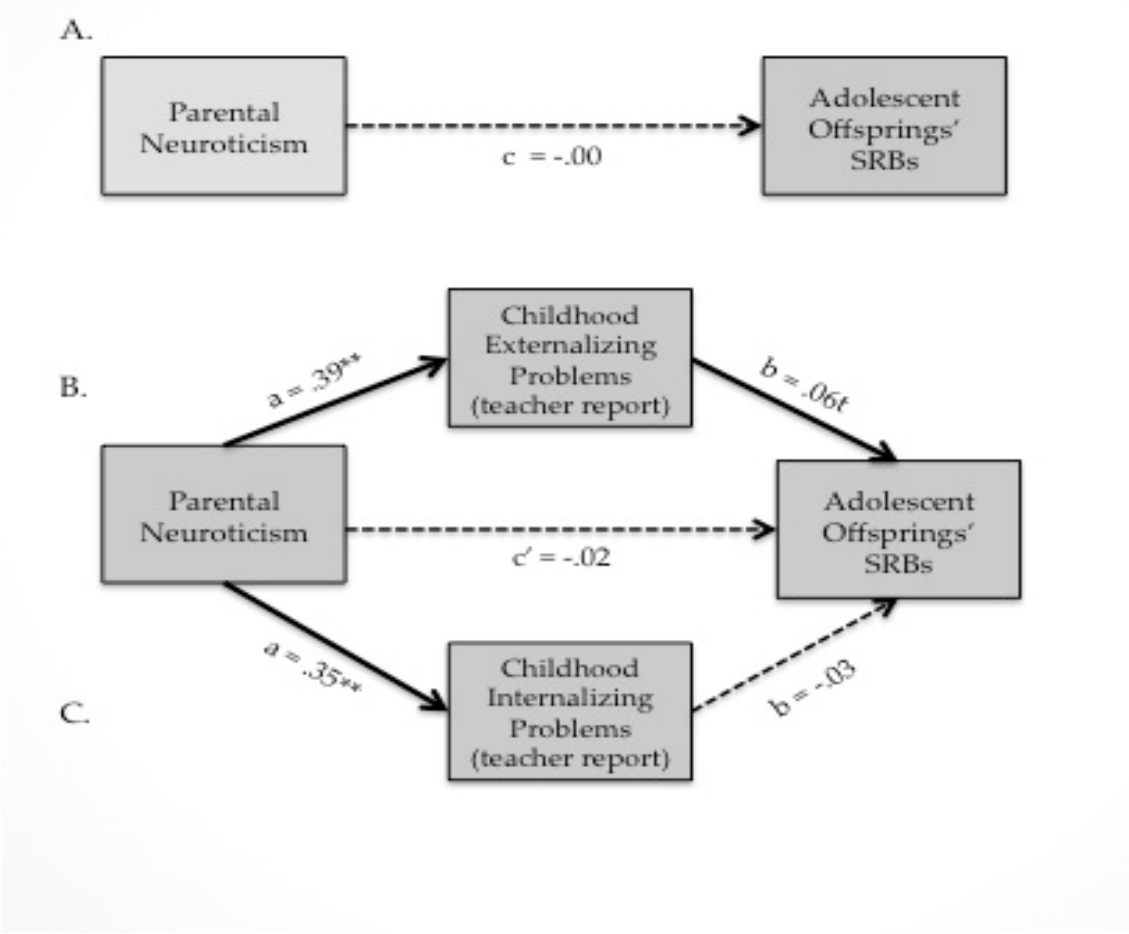
Note: * p<.05; SRB sexual risk behavior.

Figure 1. Mediation for direct and indirect effects of parental neuroticism on offspring SRBs through child problem behavior (parent report)



Panel A depicts the relationship between neuroticism in parents and SRBs in offspring, assessed approximately 10 years later. Panel B depicts the significant mediation by externalizing problems (as reported by parents) on the relationship between parents' neuroticism and offspring SRBs. Panel C depicts the relationship between internalizing problems (as reported by parents) on the association between parents' neuroticism and offspring SRBs; no mediation was observed for internalizing problems. The values in this figure are standardized path coefficients; **p<.001; *p<.05.

Figure 2. Mediation for direct and indirect effects of parental neuroticism on offspring SRBs through child problem behavior (teacher report)



Panel A depicts the relationship between neuroticism in parents and SRBs in offspring, assessed approximately 10 years later. Panel B depicts the mediation by externalizing problems (as reported by teachers) on the relationship between parental neuroticism and offspring SRBs. Panel C depicts the relationship between internalizing problems (as reported by teachers) on the association between parents' neuroticism and offspring SRBs; no mediation was observed for externalizing or internalizing problems. The values in this figure are standardized path coefficients; **p<.001; *p<.05, t non-significant trend.

CHAPTER 5. GENERAL DISCUSSION

The results from the studies comprising this dissertation add to a growing body of literature tracking the development of the OBD, a population at high risk for the development of psychopathology and other maladaptive outcomes. It has been postulated that the OBD, through genetic mechanisms and early family interactions, develop a heightened sensitivity to stress, along with problems regulating emotions and behaviors (i.e. Ostiguy et al., 2011, 2012). Research on non-psychiatric outcomes in this population help to identify markers of heightened vulnerability within this population, and can be used in the development of novel prevention strategies. To this end, the studies in the present dissertation attempted to assess risk factors in the OBD in adolescence and early adulthood and to relate these findings to childhood markers of vulnerability, as well as parent traits when the offspring were children. The first study attempted to assess different psychosocial and health-related outcomes in the OBD, including personality, coping style, smoking, suicidality, high-risk sexual behaviors (SRBs), criminality, and mental health. Results of this study showed that, as expected, the rates of affective and non-affective disorders were elevated in the OBD compared to controls. Relative to controls, OBD endorsed fewer task-oriented and more distraction (avoidant) coping strategies, and were more likely to report engaging in SRBs. Importantly, the OBD reported elevated SRBs relative to controls, irrespective of affective disorder diagnosis, suggesting that they represent a prodromal or vulnerability factor rather than sequelae of a pre-existing condition. Moreover, follow up analyses showed that, after controlling for age, gender, relationship status, and affective disorder diagnosis, parental BD diagnosis

significantly predicted SRBs. The results of this study highlight a potential risk profile for the OBD, consisting of ineffective coping strategies and risky behavior.

The second study in this dissertation followed up these results by attempting to understand SRBs in a developmental context. This study found that parents' personality in childhood, including high neuroticism, low agreeableness, and low extraversion, significantly contributed to the presence of childhood internalizing and externalizing problems. In turn, childhood externalizing behaviors predicted SRBs in the offspring 10 years later. Given that these results were found in the entire sample of OBD and control offspring, we then assessed the moderating role of BD diagnosis in parents. BD in the parents moderated the association between parents' personality and childhood externalizing behaviors, but did not moderate the association between childhood externalizing behaviors and SBRs in adolescence and young adulthood. These findings are particularly interesting because externalizing problems represent an important early marker of risk among the children whose parents have both BD and high neuroticism. These results suggest that once childhood externalizing problems have developed, they are likely to lead to SRBs, regardless of risk status. Surprisingly, given that SRBs have been suggested as a form of aggressive behavior seen more often in girls (Serbin & Karp, 2004), the above stated relationships did not differ across offspring sex. Longitudinal analyses were conducted while controlling for presence of a current affective disorder and as such findings were not likely to be artifacts of psychopathology.

Taken together, these studies highlight a risk trajectory in the OBD that includes parents' patterns of negative emotionality (as indexed by personality traits), the development of problem behavior in the offspring, and subsequent risky behaviors in the

adolescent offspring. Specifically, we found that parent and child variables interacted in middle childhood to predict sexual behavior 10 years later. Moreover, the presence of childhood externalizing problems was predictive of SRBs 10 years later, suggesting that SRBs are an extension of externalizing problems that develop earlier on in childhood. Furthermore, the association between parents' personality traits and offspring SRB were specific to offspring who displayed externalizing problems in childhood. Taken together, the findings are consistent with the view that high-risk families, through genetic vulnerability (having a parent with a mental disorder) and family social context (for example, high conflict and aggression associated with high neuroticism and low agreeableness), foster a variety of negative outcomes in offspring including difficulty responding to life stress and the engagement in risky health behaviors (Repetti, et al, 2002).

Parents' neuroticism could signify a general difficulty responding appropriately to conflict (Ellenbogen & Hodgins, 2004). As such, when conflict arises in the family, for instance in the case of addressing children's problem behavior, parents with high levels of neuroticism are likely to have difficulty navigating these interactions. This difficulty with conflict resolution could be compounded by the mood states that accompany psychopathology, creating especially stressful home environments in families with BD. The results from the second study, that parents' personality that have been previously shown to contribute to stressful home environments (i.e. high neuroticism and low agreeableness) were related to childhood behavior problems, show some support for this hypotheses. However further research examining parent-child interactions, including

observational studies that examine conflict resolution, in these households is necessary to elucidate this claim.

The literature on disruptive behavior in children suggests that it often occurs within the context of coercive parent-child cycles. In coercion theory, child non-compliance and inconsistent, hostile, irritable parenting interact to exacerbate children's problem behavior (Patterson, 1982; Patterson, Reid, & Dishion, 1992; Reid, Patterson, & Snyder, 2002). In this social learning model, bidirectional aversive interactions between parents and children serve to escalate coercive exchanges leading the parent to eventually capitulate, reinforcing children's negative behavior, and diminishing parents control over these behaviors. Evidence of coercive parent-child cycles has been seen with children as young as 24 months old (Del Vecchio & Rhoades, 2006) as well as children in middle childhood and adolescence (Patterson, 1982; Rothbaum & Weisz, 1984; Snyder & Patterson, 1995; Snyder, Schrepferman, & St. Peter, 1997). Furthermore, longitudinal studies have shown that children's externalizing behaviors increase parents' use of over-reactive, punitive disciplinary practices over time (de Haans, Soenens, Dekovic, & Prinzie, 2013; Dekovic, Janssens, & Van As, 2003; Roche, Ghazarian, Little & Leventhal, 2010;) and that such parent-child interactions during childhood predict later antisocial behavior (Moffit & Caspi, 2001; Aguilar, Sroufe, Egeland, & Carlson, 2000). Essentially, it would seem that a child who adopts externalizing strategies may exacerbate a parents' propensity towards negative emotionality, and vice versa, and that this parent-child dynamic may perpetuate the development of subsequent problem behavior.

Our findings of problem behavior are consistent with a "life-course persistent" pattern of problem behavior (Moffitt, 1993). Life course persistent patterns are thought to be influenced by gene-environment interactions and are related to the quality of parent child interactions and early socio-emotional development (Moffitt, 1993). Such patterns are differentiated from normative problem behavior that is related to the development of autonomy in young adults. Similarly, this work extends findings of heterotypic continuity in the OBD (i.e. Klimes-Dougan et al., 2010). Heterotypic continuity refers to a behavior that predicts a different form of the behavior in the same individual at a later point in time (Kagan, 1969; Rutter et al., 2006). It suggests that an underlying vulnerability may express itself in nuanced ways across development. Evidence of heterotypic continuity supports the importance of trans-diagnostic approaches which favor understanding broad domains of dysfunction that underlie disorders rather than focusing on symptoms of individual disorders (Lahey, Zald, Hakes et al., 2014; Nolen-Hoeksema & Watkins, 2011, Rutter et al., 2006).

Surprisingly, risk behavior seen in adolescents was specific to sexual behavior and did not encompass other forms of behavior such as outwardly aggressive (criminal) behavior or other health risk behaviors (smoking, self-injury). Research on SRBs in high-risk populations is still growing and as such our understanding of the meaning of such behavior is limited. Although beyond the scope of the present findings, it would appear that SRBs to occur in offspring who reside in highly stressful home environments, as indexed by the presence of parents' psychopathology and personality traits (Ellenbogen & Hodgins, 2004; Ostiguy et al., 2009). As such, one possibility is that this type of behavior exists as a form of stress-coping. Studies of individual seeking help for

hypersexual behavior show evidence of stress proneness and emotional dysregulation (Kafka, 2010; Reid, 2010; Reid, Stein, & Carpenter, 2011). Furthermore, Reid and colleagues (2013) recently showed that mindfulness, a practice exemplifying effective stress-management (Kabat-Zinn, 1982), was inversely related to hypersexual behavior in male patients after controlling for impulsivity, emotional dysregulation, and stress proneness. This research contributes to the understanding of sexual behavior as a regulatory strategy in the face of stress, however more research is needed to support this claim.

In Belsky's evolutionary model of socialization, stressors in the family environment including increased negativity and coercion lead to accelerated pubertal development, fostering earlier initiation of intercourse, more promiscuity and less stable pair bonds in offspring (Belsky, Steinberg & Draper, 1991). This theory has been supported by empirical evidence showing that greater parent-child warmth and cohesion predict later menarche and adrenarche (Ellis & Essex, 2007; Ellis, McFayden-Ketchum, Dodge, Petit, & Bats, 1999; Graber, Brooks-Gunn, & Warren, 1995; Steinberg, 1988). Additionally, harsh parenting, and child maltreatment have been shown to predict early pubertal development in daughters (Belsky, Steinberg, Houts et al., 2007; Costello, Sung, Worthman, & Angold, 2007; Tither & Ellis, 2008). It has also been demonstrated that low parental supportiveness and advanced pubertal timing are specific to children who show a higher biological susceptibility to stress (Ellis, Shirtcliff, Boyce et al., 2011). This suggests that accelerated sexual development may be especially pronounced in those who have both a biological sensitivity to context and also come from homes with compromised family functioning. As aforementioned, the OBD have evidenced a

biological sensitivity to stress compared to controls (Ellenbogen et al., 2006, 2010, 2011; Ostiguy et al., 2011; Zahn et al., 1991); furthermore, this sensitivity has been related longitudinally to measures of poor parenting in childhood (Ellenbogen et al. 2009), as well as cross-sectionally to difficulties in interpersonal interactions (Ellenbogen et al., 2013). It is possible that genetic and family environmental factors interact in the OBD to impact stress sensitivity, accelerate sexual development, and lead to important behavioral and interpersonal sequelae. As such, incorporating measures of pubertal timing into future studies of the OBD may help to elucidate the mechanisms involved in the development of risky behavior.

One key finding in the second study was that parents' neuroticism was only related to offspring problem behavior at the concurrent data collection, but showed no association with SRBs reported later on in development. Externalizing behavior problems in childhood did however predict later sexual behavior in the offspring. As such, it would appear that parents' personality during childhood serves as an early risk factor for the development of problematic behavioral patterns in offspring. This finding also suggest that preventative interventions for the OBD may be more effective if they targeted parent-child interaction in childhood, prior to the development of stable patterns of externalizing behaviors in offspring. There is growing evidence that parenting interventions can aid family functioning within high-risk families. In general, parenting programs target maladaptive behavioral (yelling, criticizing) and affective (emotional dysregulation) components of parenting, and seek to replace harsh parenting with more supportive parenting practices so as to strengthen parent-child relationships (Patterson, 1982). There is evidence that such programs can reduce children's externalizing

behaviors (DeGarmo, Patterson, & Forgatch, 2004; Wong, Gonzales, Montano et al., 2014) and improve parents' depressive symptoms (Barlow, Coren, & Stewart-Brown, 2002; Shaw, Connell, Dishion et al., 2009; Shaw, Dishion, Supplee et al., 2006) fostering positive, reciprocal parent-child interactions. Psychoeducation-based programs for families with depressed parents have also shown to be effective in reducing problem behavior in children (Beardslee & Gladstone, 2001). Furthermore, a recent review by Marsac, Donlon, and Berkowitz (2014) showed support for family interventions comprised of education about emotional reactions to stress in the enhancement of parent-child communication.

There is little research on preventative interventions in the OBD, but the few studies that have been conducted show promising results. For example, Miklowitz and colleagues (2011) conducted an open trial of family-focused therapy for high-risk youth (FFT-HR). In a sample of 13 OBD aged 9 -17 years who met diagnostic criteria for a lifetime major affective disorder, a twelve week intervention using psychoeducation and skills training was implemented with the goals of helping families 1) distinguish significant mood dysregulation from developmentally appropriate emotional reactivity 2) identify stress-related triggers of mood swings, 3) enhance family communication and problem solving, and 4) develop prevention plans to avert mood escalations and deteriorations. Youth who completed the intervention showed reduction in mood symptoms and improvement in global functioning (as assessed by the A-LIFE semistructured interview and Psychosocial Schedule; see Miklowitz et al., 2011 for details) that were maintained at the one-year follow-up assessment. Recently, Miklowitz and colleagues (2013) followed up with study using a randomized controlled trial. OBD

with a major affective disorder were assigned to either a 12-week FFT-HR intervention or an education control group of 1-2 sessions. Participants in the FFT-HR group showed a more rapid recovery from initial mood symptoms and reduced hypomanic symptoms at one-year follow-up. Furthermore, the magnitude of the treatment was greater in youth from families with high versus low expressed emotion. Although more research is needed, including consideration of issues of relapse and psychosocial qualities of those who agree to participate in the such, these findings suggest that family-based interventions targeting stress reduction, communication, and problem solving may be effective in the treatment of youth at familial risk for mood disorders.

Given the present results and those by Miklowitz et al (2013), where FFT was particularly effective among families with high expressed emotion, parent-training programs that focus on parents' high neuroticism, as well as household stress reduction, may prove particularly useful in families with BD. There are several different reasons for why parents' neuroticism may be a particularly viable target for intervention in these families. First, we have shown here and in other studies that parents' neuroticism as measured in childhood is related to concurrent and future functioning in the OBD (i.e. Ellenbogen & Hodgins, 2009; Ostiguy et al., 2012). This work extends other studies that link parents' neuroticism to poor parenting practices and indices of maladaptive parent-child interactions (see McCabe, 2014 for review). Secondly, neuroticism is gaining attention as a matter of public health significance (Lahey, 2009). This trait appears to correlate with biological, physiological, and cognitive vulnerabilities and is predictive of maladaptive functioning even in euthymic individuals (see Ormel et al., 2013). Additionally, dimensional approaches of psychopathology are leaning towards a non-

dichotomous view of personality and psychopathology in which both are represented on the same spectrum rather than considered as normal and abnormal traits, respectively (Krueger, Markon, Patrick et al., 2007). As such, monitoring and treating aspects of personality in mood disordered patients, even when they are not experiencing acute episodes, may improve individuals' functioning and overall family functioning. Importantly, preliminary work on neuroticism as a target for mental health interventions suggests that this trait is amenable to psychotherapeutic (Jorm, 1989) and psychopharmacological interventions (Tang, DeRubeis, Hollon et al, 2009).

5.1 Limitations and strengths

There are a number of limitations in the present study that also warrant discussion. The sample size was relatively small, and, as such, non-significant findings, especially regarding moderated mediation, should be interpreted with caution. Furthermore, the sample in the first study consisted of offspring from two different recruitment phases. Although there may be important differences between the subsamples, the small size of the newer sample precludes our ability to statistically assess the magnitude of these differences beyond descriptive statistics.

Another limitation was that socio-economic status was not assessed in this sample. As such we cannot make any statements about the impact of low SES on the findings within our study. This would be an important factor to consider in future research as low SES is often associated with environmental vulnerability markers such as poverty, violence and chronic stress (i.e. Taylor, Repetti, & Seeman, 1997). However, with regards to SRBs, while SES and risky sexual behaviors were highly related in the 50s and

60s (Kinsey, Pomeroy, Martin, & Gebbard, 1953; Schofield, 1965), this association is rarely seen in more recent North American samples (see Paul, Fitzjohn, Herbison, & Dickinson, 2000). Rather, family factors and school attachment have been found to be more important predictors (Paul et al., 2000). However, all analyses within this dissertation were conducted using parents' level of education as a proxy for SES and found that this did not effect the main findings. Nonetheless, SES is an important index of ecological stress and warrants further investigation in OBD samples. A previous study from our laboratory showed that parents with high levels of neuroticism also experienced greater chronic stress in the month preceding testing (Ostiguy et al., 2011). It is possible that the high neuroticism seen in these parents is a reaction to increased stress in the environment. Further studies clarifying the direction of the association between parent's neuroticism and life stress may help support interventions targeting environmental modifications and community support. Ascertaining the causation in the link between person variables, such as neuroticism, and environmental stress may lead to the development of more effective interventions and community supports for high-risk populations.

The studies within this dissertation were the first to our knowledge to examine sexual risk behaviors in the OBD. As such, they provide foundational knowledge upon which to examine problematic sexual behavior in future studies of the OBD. Furthermore, the first study was one of only two to date that has looked at the "Big Five" personality traits in the OBD. Rothen and colleagues (2009) used the NEO-PI-R to examine trait neuroticism, extraversion, and psychoticism in the OBD and offspring of parents with unipolar depression (O-UNI). This study found that affected OBD and O-

UNI scored higher on the neuroticism dimension; affected OBD also scored higher on the psychoticism dimension, suggesting personality changes could be a consequence rather than a precursor of mood episodes. The present study did not find any personality difference between the OBD and offspring of parents with no mental disorder. These negative findings may be meaningful, in that they suggest that changes in personality may only develop in adulthood. It may be that the sample in the present study was too young to be able detect stable personality traits. Additionally, the presence of traits such as high neuroticism may co-occur with the development of affective disorders and thus may not be as prominent in those who are without a major affective disorder or who do not have a considerable history of mood disorder episodes. Further studies are needed to clarify the relationship between personality and mood disorders. Another major strength of this set of studies is the use of diagnostic interviews of parents and children rather than self-report questionnaires, allowing for more objective information on indices of psychopathology. Finally, the second study presented within this dissertation was based on rare 10-year prospective longitudinal data. Presently only a few similar samples exist (see Duffy, 2012; Hillegers et al., 2005; Klimes-Dougan, et al., 2010). Longitudinal studies allow researchers to assess the association among variables across time, providing unique information on developmental factors and individual growth and change, and are thus integral to our understanding of the OBD.

5.2 CONCLUSIONS

Overall, the findings reported in this dissertation suggest a pattern of relative continuity of risk across generations, defined by a trajectory of high emotionality and disagreeableness in the parents, offspring externalizing problems in childhood, and sexual

risk behaviors in late adolescence and early adulthood. The present findings suggest that preventative interventions implemented in childhood in high-risk families could be used to target maladaptive development and interrupt the intergenerational transmission of risk from parents to children. In addition, the findings support the view that parents' neuroticism represents an important vulnerability factor for their offspring's development that could be targeted in future intervention programs. Taken together, the results reported above imply a pattern of continuity of externalizing problems in the OBD that are influenced by parents' personality traits, and that could be amenable to well-timed, well-targeted interventions.

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