# Parenting behaviors and the prevention of psychopathology in the offspring of parents with bipolar disorder

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**ABSTRACT**

Parenting behaviors and the prevention of psychopathology in the offspring of parents with bipolar disorder

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The offspring of parents with bipolar disorder (OBD) are at elevated risk for mental health problems throughout the lifespan. In addition to genetic factors, environmental risk is purported to be associated with these negative outcomes. The current dissertation was designed to both examine and intervene in the relations between exposure to distinct aspects of the caregiving environment in middle childhood and psychopathology in the OBD. In the first study, concurrent and longitudinal data were used to investigate if levels of support (emotional warmth), structure (organization and consistency), and control (disciplinary strategies) provided by parents in middle childhood mediated the relation between having a parent with bipolar disorder and offspring mental health. Relative to support, structure provided by parents in the home was found to have robust effects on emotional and behavioral problems in middle childhood, while control promoted psychological adjustment in the OBD up to 12 years later. In the second study, the efficacy of a 12-week program, entitled Reducing Unwanted Stress in the Home (RUSH), was examined using a quasi-experimental design with an assessment-only control group. The program, based on empirical research in the OBD, was designed to improve the quality of the caregiving environment in childhood and to promote effective coping skills and resilience among the OBD, with the end goal of reducing their risk of adverse mental health outcomes as they develop. Assessments were conducted at four time points up to six months following the end of the RUSH program, during which parent-child interaction quality (parental positivity and negativity, and dyadic mutuality) was measured in the laboratory. Participation in the RUSH program was found to decrease rates of parent- and teacher-reported internalizing symptoms in the OBD six months later via pre-to-post intervention gains in parental negativity and positivity, respectively. Together, these studies suggest that suboptimal childrearing environments in families with a parent having BD represent a putative causal mechanism for internalizing and

externalizing problems among the OBD. These data further imply that, even for highly heritable disorders like bipolar disorder, manipulations of the caregiving environment via short and targeted intervention can be of benefit.

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## Contribution of Authors

This thesis consists of two manuscripts. The relative contributions of my colleagues to each manuscript is outlined below:

**Study 1:** Iacono, V., Beaulieu, L., Hodgins, S., & Ellenbogen, M.A. (2017). Parenting practices in middle childhood mediate the relation between growing up with a parent having bipolar disorder and offspring psychopathology from childhood into early adulthood. *Development and Psychopathology,* 1-15. doi:10.1017/S095457941700116X

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

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Vanessa Iacono and Mark Ellenbogen designed the study. Vanessa Iacono, Lisa Serravalle, Alexa L. Wilson, Mark Anthony Orlando, and Virginia Tsekova collected the data. Vanessa Iacono, Lisa Serravalle, and Mark Anthony Orlando conducted the clinical interventions. Lisa Serravalle and Virginia Tsekova coded the behavioral data. Vanessa Iacono conducted the statistical analyses and wrote the first draft of the manuscript. Vanessa Iacono and Mark Ellenbogen edited subsequent versions of the manuscript. All authors approved the final manuscript.

## Table of Contents

## List of Figures

## List of Tables

## Chapter 1: General introduction

Growing up with a parent having a serious mental illness has been associated with a host of adverse outcomes from childhood into adulthood (Dean et al., 2010; Gottesman, Laursen, Bertelsen, & Mortensen, 2010; McLaughlin et al., 2012). In particular, the offspring of parents with bipolar disorder (OBD), through a complex transaction between genetic and environmental factors, are at risk for developing a number of socio-emotional, behavioral, cognitive, academic, and occupational problems throughout their lifespan (Bella et al., 2011; Mowbray & Mowbray, 2006; Nijjar, Ellenbogen, & Hodgins, 2014; Whitney et al., 2013). Unfortunately, the availability of psycho-social prevention programs for the OBD is scarce and remains largely limited to programs geared towards adolescent youth already presenting with prodromal mood symptoms (see Miklowitz & Chung, 2016 for a review).

The goal of this thesis is two-fold. First, this thesis will explore parenting practices in middle childhood and how they relate to developmental outcomes in the OBD approximately 12 years later, as the offspring enter late adolescence and early adulthood. Specifically, suboptimal parenting practices provided by parents with bipolar disorder (BD) will be described as key elements of the childrearing environment in middle childhood that contribute to risk for internalizing and externalizing symptoms among the OBD as they mature. The use of a prospective design is one effective method of tracking the development of high-risk youth and gaining insight into the environmental factors that perpetuate risk trajectories. Based on the results of the first dissertation study and other studies of the OBD (e.g., Calam, Jones, Sanders, Dempsey, & Sadhnani, 2012; Ellenbogen & Hodgins, 2004; 2009; Lau et al., 2018) that highlight the need for preventative interventions in this population, the second study in this thesis will explore efficacy for a novel psycho-social prevention intervention program aimed at thwarting the early development of emotional and behavioral problems among the OBD via positive alterations in parent-child interaction quality. Guiding theoretical frameworks for this research lie in the diatheses-stress (Rosenthal, 1963; Zuckerman, 1999) and transactional (Cicchetti & Toth, 1997) models of psychopathology. Taken together, these models posit that mental illness is the product of an individual vulnerability that interacts with a certain degree of exposure to environmental stress that, in turn, result from ongoing bi-directional and reciprocal influences between offspring and the contexts within which they are raised. The purpose of this introductory

chapter is to elucidate risk pathways to mental health problems among the OBD and review the current state of the prevention intervention literature.

**BD and psychiatric and non-psychiatric outcomes among the OBD**

BD is a chronic and episodic affective disorder characterized by bouts of mania, hypomania, and depression. Three distinct forms of the disorder exist, including BD-1 ("traditional" view of BD, requiring at least one lifetime episode of mania), BD-2 (requiring at least one lifetime episode of both hypomania and major depression), and cyclothymic disorder, which is reserved for individuals who present with recurrent experiences of hypomania and depression, but without ever meeting full diagnostic criteria for either condition (Diagnostic and statistical manual of mental disorder, 5th ed. (DSM-5); American Psychiatric Association, 2013). A recent review of epidemiological and clinical studies across eleven countries indicates that approximately 1% of the general population will meet full diagnostic criteria for BD-1 or BD-2 during their lifetime, with an additional 1.4% showing subthreshold symptoms of BD (Merikangas et al., 2011). At least half of individuals who eventually develop some form of BD report onset before the age of 25 years, with mean ages at onset falling between 18 and 21 years (Merikangas et al., 2011).

Lifetime prevalence rates across all forms of BD are substantially higher among the OBD than the offspring of parents having no mental disorder. Compared to low-risk offspring, the OBD are not only about ten times more likely to develop a form of BD in their lifetime, but also tend to experience their first manic or depressive symptoms earlier during the course of adolescence (e.g., Axelson et al., 2015; Birmaher et al., 2009; Mesman, Nolen, Reichart, Wals, & Hillegers, 2013; Singh et al., 2007). Among the OBD who eventually develop bipolar disorder, important societal and economic costs are observed, including the heavy use of health services and loss of productivity in the workplace (see Dean, Gerner, & Gerner, 2004 for a review), high premature mortality rates (e.g., due to suicide or co-occurring medical causes; Angst, Stassen, Clayton, & Angst, 2002; Laursen, Munk-Olsen, Nordentoft, & Mortensen, 2007), and elevated number of comorbid axis-I and axis-II psychiatric disorders (Fan & Hassel, 2008; Merikangas et al., 2011). In fact, rates of other internalizing and externalizing psychopathologies are equally concerning among the OBD, with about 60% of the OBD meeting diagnostic criteria for an anxiety, substance use, attentional, or oppositional defiant disorder at some point in their lifetime. By young adulthood, approximately 30- 50% of the OBD will have developed an affective

disorder compared with only 10% of offspring of parents with no affective disorder (ONAD; see DelBello & Geller, 2001; Rasic, Hajek, Alda, & Uher, 2013 for reviews). This risk has been found to increase two-fold when offspring have two, relative to only one, biological parents with BD (Birmaher et al., 2009; Vandeleur et al., 2012).

In addition to poor mental health outcomes, the OBD display elevated risk for a host of non-psychiatric problems throughout the lifespan. For example, a number of neurocognitive and executive dysfunctions have been described in the OBD compared to their low-risk counterparts, including impairments in mental flexibility, planning, problem-solving, verbal fluency, spatial memory, and sustained attention (Meyer et al., 2004; Klimes-Dougan, Ronsaville, Wiggs, & Martinez, 2006; Maziade et al., 2009). Disturbances in reality testing (Narayan, Allen, Cullen, & Klimes-Dougan, 2013), as evidenced by the presence of psychotic symptoms, thought problems, and cognitive disruptions, and a tendency toward sensation seeking (Chang, Blasey, Ketter, & Steiner, 2003; Jones, Tai, Evershed, Knowles, & Bentall, 2006) and risk-taking behavior (Nijjar et al., 2014) have also been reported in this population. As it pertains to interpersonal competence, the literature is presently mixed, with some researchers having found evidence for impaired psychosocial functioning and impoverished peer networks among the OBD (e.g., Bella et al., 2011; Ostiguy et al., 2009), while others have not (e.g., Anderson & Hammen, 1993; Reichart et al., 2007). Nonetheless, it is likely that deficits in cognitive, executive, academic, and interpersonal functioning contribute to maladaptive development among the OBD, further increasing their susceptibility to mental health problems as they mature.

**Intergenerational risk for mental disorders among the OBD: Overview of contributing factors**

Current clinical staging models suggest that BD likely progresses in a predictable clinical sequence from non-specific emotional and behavioral difficulties in childhood (e.g., attention, sleep, disruptive behavioral, and anxiety disorders) followed by specific minor to major mood psychopathology from late adolescence into early adulthood (Duffy et al., 2010; 2014; 2017; 2018). This is consistent with a recent review of the literature on bipolar switching (i.e., eventual conversion of mood symptoms to full-blown BD), which highlights the experience of non-specific mood syndromes, multiple depressive episodes, and subthreshold manic symptoms as key clinical predictors for BD (Fiedorowicz, Endicott, & Akiskal, 2013).

Interestingly, while risk is elevated compared to healthy community samples, the majority of the OBD will not develop BD in their lifetime. Rather, as previously alluded, it is the prevalence of other mood disorders and axis-I conditions (e.g., substance abuse, psychotic, or anxiety disorders) that is even greater among the OBD, with a two-to-four-fold increase in rates of other major affective disorders or other axis-I disorders relative to healthy controls from childhood into adulthood (Rasic et al., 2013). This suggests that growing up with a parent having BD conveys heightened risk for psychiatric illness throughout the lifespan; although, not specifically for BD. Likewise, not all children who have a parent with BD will grow up to experience adverse psychopathological outcomes. Well-known to the field of developmental psychopathology (Cicchetti & Rogosch, 1996), research to date thus reflects the relevance of the constructs of "multifinality" (i.e., similar developmental trajectories leading to different outcomes) and "equifinality" (i.e., different developmental trajectories leading to the same outcome) in understanding developmental outcomes among the OBD. Ultimately, the pathogenesis of BD remains ill-understood. Most likely, risk for maladaptive development among the OBD is conveyed through a series of complex and multifaceted mechanisms, including genetic and environmental factors, which interact over time to impact brain function and structure, and behavior (Brietzke et al., 2012).

***Genetic basis of BD***

Family and twin studies have highlighted the significance of genetic factors in conveying vulnerability to BD. Over two decades of research (see Barnett & Smoller, 2009; Craddock & Jones, 1999; Craddock & Sklar, 2013; Smoller & Finn, 2003 for reviews) has identified risk for BD to be strongest in families of probands with BD, with first degree relatives being approximately eight times more likely to develop BD in their lifetime compared to unrelated members of the general population. This is consistent with research showing a positive family history of affective illness to be common among patients with BD, as is a family pedigree of BD in patients whose depressive episodes eventually transition to mania (Fiedorowicz, Endicott, Solomon, Keller, & Coryell, 2012; Rende et al., 2005). Estimates of heritability (i.e., proportion of variation in a disorder that is due to genetic rather than environmental contributions; where 100% would indicate complete heritability) derived from three of the largest twin studies to date are elevated and have ranged from 79%-93% depending on research design, sample characteristics, and diagnostic decision making (Kendler, Pedersen, Neale, & Mathé, 1995;

Kieseppä, Partonen, Haukka, Kaprio, & Lönnqvist, 2004; McGuffin et al., 2003). Monozygotic concordance rates (i.e., for twins who share 100% of their genes) fall between 38.5%-43% compared to 4.5%-5.6% for dizygotic twins (i.e., for twins who share only 50% of their genes), with higher concordance rates reflecting those investigations that have included all forms of BD (relative to BD-1 only). Although genetics play an important role in the transmission of BD across generations, no single gene has been – or will likely ever be – identified as producing the cluster of symptoms that is characterized as BD. Rather, data derived from well-designed genome-wide association studies (e.g., Baum et al., 2008; Ferreira et al., 2008; Sklar et al., 2008) suggest that the genetic basis of BD more likely stems from many genes of small effects that, in combination, increase risk for the development of BD. Alternatively, some researchers have argued that genetic susceptibility to BD may be best understood via the inheritance of specific biological traits (i.e., "endophenotypes"; Gottesman & Gould, 2003) rather than the direct transmission of genes associated with the disorder per se. One such area of growing interest has been the identification of neural patterns associated with deficits in socio-emotional information processing (e.g., Wiggins et al., 2017). Ultimately, identification of genetic risk factors remains difficult due to the heterogenous nature of BD and need for increasingly large research samples (Craddock & Sklar, 2013).

***Socio-emotional information processing and the search for brain-based markers of risk***

The ways in which individuals process specific social and emotional information influences their overall level of adjustment and mental health (e.g., Etkin & Wager, 2007; Gotlib et al., 2004). There is growing evidence to suggest that the OBD may process socio-emotional information differently than their low-risk counterparts. For example, Brotman and colleagues (2008a, 2008b) found that the OBD have greater difficulty correctly labeling both positive and negative emotions depicted in images of faces, and that they also require more salient emotional information in order to accurately identify pictures of facial affect relative to healthy controls. An attentional bias towards emotional (Bauer et al., 2015) and socially threatening words (Gotlib, Traill, Montoya, Joormann, & Chang, 2005), and better recall for negative self-descriptions, have also been reported in the OBD relative to ONAD samples (Gotlib et al., 2005). Similar patterns of deficits have been observed in patients with BD (e.g., Venn et al., 2004) and in their unaffected adult siblings (e.g., Brand et al., 2012).

Consistent with these behavioral findings, functional neuroimaging research has identified altered patterns of brain activation in the ventrolateral and dorsolateral prefrontal, cingulate, and limbic regions (i.e., areas associated with emotional processing, attentional control, response inhibition and initiation, reward, and motivation) during tasks of face emotion processing in pediatric (Pavuluri, O'Connor, Harral, & Sweeney, 2007; Rich et al., 2008) and adult (Houenou et al., 2011; Morris, Sparks, Mitchell, Weichert, & Green, 2012) samples of patients with BD, as well as those at familial risk (Surguladze et al., 2010; Wiggins et al., 2017). As it pertains more specifically to the OBD, studies using tasks of implicit face emotion processing (i.e., wherein the participant is required to respond to non-emotional content while being simultaneously exposed to emotional stimuli) have demonstrated greater neural activation in regions of the prefrontal cortex relative to healthy controls in reaction to happy facial expressions, while reduced neural activation in the amygdala and inferior frontal gyrus (part of the limbic and prefrontal brain regions, respectively) has been described in relation to angry facial expressions (Brotman et al., 2014). In turn, impaired neural activation has been shown to accurately discriminate between adolescent OBD and ONAD (Mourao-Miranda et al, 2012). Further, aberrant patterns of cortico-subcortical connectivity, a neural circuit implicated in voluntary emotional regulation, during resting state and reward processing (Singh et al., 2014a; 2014b), as well as in response to both positive and negative facial emotion (Ladouceur et al., 2013; Manelis et al., 2015) have been reported in the OBD. A number of neuroanatomical particularities also characterize the OBD compared to their low-risk counterparts, including grey matter abnormalities in the inferior frontal gyrus, left anterior thalamus, left parahippocampal gyrus, and left hippocampus (see Nery, Monkul, & Lafer, 2013 for a review).

Taken together, there is growing evidence to indicate that the OBD differ from low-risk controls in brain structure and function, demonstrating a pattern that may contribute to dysregulation that is at least partly associated with observed impairments in the processing of socio-emotional information. Importantly, deficits in the brain systems associated with face emotion processing may represent markers of risk among the OBD; although, additional prospective research tracking the development of the OBD as they mature and investigations into the heritability of face emotion processing in probands of patients with BD are still needed to establish whether impaired face emotion processing is an endophenotype for BD (Brotman et al., 2008a). Albeit speculative, it is possible that dysfunction within these brain regions underlies

other regulatory functions that contribute to mental health problems in the OBD, including areas involved in extreme mood change and emotion regulation (e.g., Ellenbogen, Schwartzman, Stewart, & Walker, 2002).

***Biological sensitivity to stress: The hypothalamic-pituitary-adrenal system***

The functioning of the hypothalamic-pituitary-adrenal (HPA) system and the transmission of risk alleles (i.e., one of two or more alternative forms of a gene) associated with biological sensitivity to stress is another risk factor that has long been postulated to play an important role in the pathogenesis and pathophysiology of BD (Daban, Vieta, Mackin, & Young, 2005; Deshauer, Grof, Alda, & Grof, 1999). Specifically, the HPA system is known for regulating and coordinating a number of bodily processes through the production and release of the hormone cortisol (McEwan, 2007). Namely, the HPA system is responsible for a cascade of endocrine events that starts with the release of corticotrophin-releasing hormone (CRH) from the hypothalamus. In turn, CRH binds to CRH receptors on the anterior pituitary gland, which stimulates release of adrenocorticotropic hormone. Adrenocorticotropic hormone then travels to the adrenal cortex where cortisol is produced and released into the blood stream. The basal activity of the HPA system adheres to relatively stable circadian and ultradian rhythms characterized by a sharp rise in cortisol levels in the first 30 minutes after awakening followed by a gradual reduction in cortisol concentration (Nicolaides, Charmandari, Chrousos, & Kino, 2014). In response to stress or challenge, cortisol is released for an extended duration, until its levels are reduced through cortisol-activated negative feedback. Further, through its homeostatic and allostatic influences, the HPA system can elicit change in gene expression and in the function and structure of the central nervous system over the lifespan (de Kloet, Karst, & Joels, 2008; Goosens & Sapolsky, 2007; Sapolsky, Romero, & Munck, 2000).

Results from a recent meta-analysis conducted by Murri and colleagues (2016) linked BD to a number of abnormalities in the HPA system during both illness episodes and in a euthymic state, including elevated secretion of cortisol upon awakening and in response to psychosocial stress. Evidence also exists to indicate that HPA dysregulations might impact the clinical course of BD, in such a way that chronic HPA hyperactivity may be positively correlated with onset and recurrence of mood and psychotic symptoms. Similarly, HPA hyperactivity has been repeatedly demonstrated in the OBD (Ellenbogen et al., 2006; 2010; Ostiguy, Ellenbogen, Walker, Walker, & Hodgins, 2011); although, less consistently so among other unaffected first-degree relatives of

patients with BD. According to Murri and colleagues (2016), such inconsistencies in findings weaken the hypothesis that dysregulated HPA functioning may represent an endophenotype for the development of BD, but instead highlight the role of gene-environment interactions in shaping the transition to full-blown mood disorders among the OBD. This hypothesis is partly supported by retrospective and longitudinal data linking HPA hyperactivity in the OBD to exposure to adverse environments in childhood, such as the experience of abuse or neglect (Watson et al., 2007), and suboptimal parenting practices (Ellenbogen & Hodgins, 2009), as well as heightened risk for the subsequent development of serious mood problems (Ellenbogen, Hodgins, Linnen, & Ostiguy, 2011). Gene-environment interactions are discussed in further detail at a later point in Chapter 1.

***Summary of the literature on genetics and the transmission of neurobiological markers of risk***

In sum, despite the large role played by genetic factors, it is improbable that the direct transmission of genes associated with BD is responsible for the degree of susceptibility to the disorder observed across multiple generations of a same family. At least as it pertains to the OBD, it is more likely that they inherit traits or vulnerability markers that increase their risk for psychological maladjustment throughout the lifespan. Neurobiological and neuroanatomical abnormalities in the brain regions that are involved in face emotion processing and underlie extreme mood change and emotion regulation may represent one such candidate endophenotype; although, further longitudinal research is needed for this to be determined. Dysregulations within the functioning of the HPA system has been proposed as another neurobiological correlate of illness progression in BD. Conversely, as research conducted on the OBD has shown greater consistency in describing HPA dysfunction than those involving first-degree relatives, exposure to stressful environments in childhood, such as suboptimal childrearing environments, may be responsible for the intergenerational transmission of HPA abnormalities that underlie risk for mood disorders among the OBD.

***The role of the childrearing environment***

Caregiving environments in childhood are well-known predictors for a range of behavioral and psychosocial outcomes. Evans (2006) reviewed the impact of the physical environment within which a child is raised, including levels of noise and crowdedness, exposure to environmental contaminants, and housing and neighborhood quality, and noted negative repercussions in terms of socio-emotional and cognitive development, achievement motivation,

and psychophysiology. Suboptimal physical environments are disproportionately represented in families with low socio-economic status, another well-established environmental risk factor for abnormal mental health trajectories throughout the lifespan (see Bradley & Corwyn, 2002 for a review). As most of the skills required for healthy physical and socio-emotional development are acquired via the parent-child relationship (Bornstein, 2002), parenting strategies and parent-child interaction quality have also received much empirical attention. Consistently, an authoritative parenting style, which integrates parenting practices intended to optimize levels of both responsiveness (sensitivity, warmth, and involvement) and demandingness (disciplinary control, monitoring of activities, and structuring) (Maccoby & Martin, 1983), has been associated with secure attachment relationships between parents and their offspring in childhood, adolescence, and adulthood (Doinita, & Maria, 2015; Karavasilis, Doyle, & Markiewicz, 2003), as well as with psychological well-being in youth (e.g., Larzelere, Morris, & Harrist, 2013; Piko & Balazs, 2012).

As it pertains to the OBD, they inherit both genes and a shared family environment from their parents, exposing them to a parent who can periodically become psychotic, dysfunctional, neglectful, or even abusive as a consequence of their mental health status. In fact, in a recent study by Goodday and colleagues (2018), the severity, duration, and timing of offspring's exposure to parental BD in early childhood was associated with risk for mood and non-mood disorders in the OBD. To date, two relatively distinct lines of research have endeavored to describe risk processes within the family environment of the OBD: studies characterizing overall family functioning as that of a "unit" and those focusing on dyadic relationships within the family. Chang and colleagues (2001) were the first research group to report on general dynamics among families with one or both parents having BD, noting lower levels of cohesion and organization, as well as elevated conflict relative to normative population means. Similar results were found in a number of subsequent studies comparing the global functioning of families with a parent having BD to controls using the parent-report Family Environment Scale, a questionnaire measuring the overall social and environmental characteristics of families (e.g., Barron et al., 2014; Ferreira et al., 2013; Lau et al., 2018; Romero, DelBello, Soutullo, Stanford, & Strakowski, 2005). Elevated levels of marital discord and separation (Dore & Romans, 2001; Lam, Donaldson, Brown, & Malliaris, 2005), parental absenteeism (e.g., due to hospitalizations; Pini et al., 2005), and chaos, disorganization, and instability within the household also appear to

distinguish families with and without a parent having BD (Calam et al., 2012; Ellenbogen & Hodgins, 2009). As it pertains to the more micro-level process of parent-child interactions, negative communication styles and affectivity, lack of sensitivity and responsiveness, and increased disengagement, disorganization, irritability, tension, and unhappiness have been described within the context of a parent having BD (Davenport, Zahn-Waxler, Adland, & Mayfield, 1984; Inoff-Germain, Nottelmann, & Radke-Yarrow, 1992; Meyer et al., 2006; Radke-Yarrow, Nottelmann, Belmont, & Welsh, 1993; Tarullo, DeMulder, Martinez, & Radke-Yarrow, 1994; Vance, Huntley, Espie, Bentall, & Tai, 2008). Evidence of poor parental bonding and insecure attachment styles in early childhood (Radke-Yarrow, Cummings, Kuczynski, & Chapman, 1985) and adolescence (Erkan, Gencoglan, Akguc, Ozatalay, & Fettahoglu, 2015; Lau et al., 2018) further confirms the existence of compromised parent-child interactions among the OBD.

***Impaired childrearing environments and psychopathology among the OBD***

Suboptimal childrearing environments have been robustly documented in families with a parent having BD. Conversely, research into the associations between BD in a parent, exposure to impaired caregiving, and illness onset among the OBD is relatively new. Earlier studies focused on the role of expressed emotion within the family (i.e., critical, hostile, or emotionally over-involved attitudes held by family members towards a relative suffering from a mental illness; Vaughn & Leff, 1976), which has been associated with heightened interpersonal stress during remission (Simoneau, Miklowitz, & Saleem, 1998) and an increased probability of relapse up to nine months later among patients with BD (Miklowitz, Goldstein, Nuechterlein, Snyder, & Mintz, 1988). Among the OBD, retrospective investigations have supported a positive association between dysfunctional parent-child relationships in childhood and adolescence, and adult BD (Alnaes & Torgersen, 1993; Rosenfarb, Becker, & Khan, 1994). Bi-directional, cross-sectional correlations have also been repeatedly described between heightened conflict and poor cohesion and organization within the childrearing environment, and the experience of emotional and behavioral problems from toddlerhood into late adolescence (Calam et al., 2012; Freed et al., 2015; Lau et al., 2018). Using a longitudinal design spanning approximately 20 years, Meyer and colleagues (2006) linked extreme displays of negative affect and attitudes among mothers with BD during early childhood interactions with their offspring to the likelihood of developing BD in young adulthood. This association was retained over and above the direct influence of having a

mother with BD, indicating that aspects of the childrearing environment in earlier childhood may be unique predictors of later mental health problems among the OBD. Additionally, there exists evidence to suggest that the presence of an axis-I pathology among the OBD can further contribute to dysfunctional caregiving environments in families with a parent having BD. For example, Zahn-Waxler, McKnew, Cummings, Davenport & Radke-Yarrow (1984) observed elevated hostility and low altruism in two-year-old OBD during social interactions. More recently, Ferreira and colleagues (2013) reported a positive association between the presence of an axis-I psychiatric disorder in the OBD and levels of control (i.e., number of rules and procedures) provided by parents to manage family life on a daily basis, possibly representing an attempt to cope with the alterations that occur within the functioning of the family unit when both a parent and its offspring suffer from a mental illness.

Only two cross-sectional studies to date have attempted to further clarify the role of impaired caregiving on the mental health of the OBD by investigating indirect pathways between growing up with a parent having BD and offspring's experience of psychological symptoms. In a study by Schudlich and colleagues (2008), elevated family conflict was shown to underlie the relation between having a parent with BD and offspring's current BD during adulthood. Conversely, Lau and her research team (2018) failed to find significant mediation between having a parent with BD and concurrent mental health problems in the OBD via the quality of the childrearing environment; defined as levels of family emotional bonding and parental warmth and support. One hypothesis is that the presence of chaos, disorganization, and instability within the home environment, relative to the absence of warmth, bonding, and nurturance, may be particularly relevant for predicting adverse psychopathological outcomes among the OBD. This conjecture is supported by research attesting to the presence of neurocognitive deficits (e.g., Maziade et al., 2009) and neurobiological abnormalities (e.g., Ellenbogen et al., 2010; Ladouceur et al., 2013) in unaffected OBD. In turn, there is preliminary evidence to indicate that exposure to disorganized and chaotic home environments in middle childhood modulate cortisol reactivity (Ellenbogen & Hodgins, 2009), and cross-sectionally predict weakened frontostriatal connectivity (Singh et al., 2014) in the OBD. Similarly, a caregiving environment characterized by high levels of organization, consistency, and parental limit setting and scaffolding has been shown to foster the emergence of higher-order cognitive functions in typically-developing youth (Hughes & Ensor, 2009; Schroeder & Kelley, 2009; 2010); although, this has yet to be explicitly

investigated in the OBD. Taken together, these data support the evolving hypothesis that unstructured, disorganized, and chaotic childrearing may represent a unique environmental mechanism by which susceptibility to psychopathology is increased among the OBD.

**Is the risk for mental disorders among the OBD best understood as a gene-environment interplay?**

The etiology of BD and risk for maladaptive development among the OBD is complex and multi-factorial. Although relatively understudied compared to other highly heritable psychiatric disorders (e.g., schizophrenia, major depression; see Uher, 2014 for a review), prevailing hypotheses suggest that susceptibility to BD and other mental health problems among the OBD may be the consequence of a gene-environment interaction. A gene-environment interaction refers to the differential influence that exposure to an environment can have in individuals with different genotypes (Ottman, 1996). The interaction can be expressed in a diathesis-stress framework, which anticipates stronger correlations between genotype (diathesis) and outcome under negative (stressful) relative to positive environmental conditions (Rosenthal, 1963; Zuckerman, 1999).

Gene-environment interactions have already been established for a broad range of physical (e.g., colorectal cancer, HIV, obesity), behavioral (e.g., antisocial behavior), and emotional (e.g., anxiety, depression) problems (see Rutter, Moffitt, & Caspi, 2006 for a review). In BD, for example, Hosang and colleagues (2010) found that chronicity and severity of mood episodes following exposure to stressful life events depended on whether or not adult individuals with BD carried the brain-derived neurotrophic factor met allele. Likewise, the Paranoxonase 1 (a hydrolytic antioxidant enzyme) QQ genotype was shown to differentially moderate the effects of smoking (which was operationalized as an environmental stressor in this study) on the odds of having BD or major depression in adulthood (Bortolasci et al., 2014). Only one study to date investigated but failed to find evidence that the brain-derived neurotrophic factor met allele interacted with exposure to childhood sexual abuse to predict clinical course in a sample of adults with BD (Miller et al., 2013). However, the authors attributed this non-replication to the use of an insufficiently large sample.

Regarding the OBD, it is possible that genetic liability to emotional and behavioral problems transmitted from parent to offspring (e.g., transmission of neurobiological abnormalities) is exacerbated (or activated) by exposure to stressful childrearing environments

(e.g., lacking in structure, organization, and stability) that result from growing up with a parent having BD. As aforementioned, in a cross-sectional study conducted by Singh and colleagues (2014a), frontostriatal connectivity during resting state was shown to be negatively correlated with levels of parent-reported family chaos in a healthy sample of pre-adolescent OBD. Similarly, suboptimal levels of organization and consistency provided by parents in middle childhood have been linked to increased HPA reactivity in an adolescent sample of unaffected OBD that, in turn, predicted the development of major mood problems about two years later (Ellenbogen et al., 2009; 2011). The presence of a gene-environment interaction is further supported by the large "heritability gap" for BD, which refers to the fact that no single genetic variation seems able to explain much of the heritability of BD (Uher, 2009; 2013). Rather, it is likely that shared environmental factors are included in and overestimate heritability estimates from twin studies, while failing to contribute to heritability estimates derived from unrelated individuals. This, ultimately, proposes a substantial role for gene-environment interactions in the etiology of BD and vulnerability to abnormal development among the OBD (see Uher, 2014 for a review). However, gene-environment interactions have never been directly investigated in the OBD.

**Conclusions from the literature on risk factors identified in the OBD**

Research into the genetic and environmental factors associated with risk for mental disorders and other negative outcomes among the OBD indicates that the pathways to maladaptive development in this population are complex. While the nature and extent of each risk factor's unique contribution continues to be the topic of active investigation, one possibility is that a gene-environment interaction - namely, the diathesis between a genetically-transmitted trait(s) and exposure to suboptimal childrearing environments (stress) – may describe susceptibility to psychopathology among the OBD. Despite the large role that genetic factors play in the development of an affective disorder in the OBD, there are no known preventative strategies to directly alter genetic risk. Thus, a focus on risk factors that can be altered, such as the caregiving environment, might represent an important strategy to change the gene-environment interactions that influence the development of the OBD.

**Contemporary prevention intervention**

Early prevention interventions conducted in schools and community settings were largely based on principles of information dissemination and fear arousal, but have since been deemed

insufficient for changing the attitudes, intentions, and behaviors of youth (Catalano, Hawkins, Berglund, Pollard, & Arthur, 2002). Today, intervention programs rooted in the philosophy of prevention science attempt to either reduce risk factors (i.e., individual or environmental variables associated with an increased likelihood that an adverse outcome will occur, such as the experience of stressful life events or having a parent with a mental illness) and/or promote protective factors (individual or environmental safeguards that enhance a person's resistance to risk and promote adaptation such as effective coping skills; Durlak, 1998; Small & Memmo, 2004). Contemporary prevention programs can also be categorized into one of three types based on the nature of the population being served (Weissberg, Kumpfer, & Seligman, 2003). Universal prevention programs target the general public (or an entire population), while selective prevention programs focus on unaffected individuals or subpopulations that demonstrate the biological, psychological, or environmental risk factors that render them at elevated risk for the targeted negative outcome. Thirdly, indicated prevention programs target high-risk individuals that show detectable symptoms predictive of a disorder (e.g., non-specific mood problems), but do not yet present with the full-blown disorder (e.g., BD).

**Prevention of mental disorders in the OBD**

Given the OBD's vulnerability to psychosocial adversity throughout the lifespan - and the elevated personal, familial, and societal burden associated with the development of mental disorders in high risk youth - there is a growing need for organized prevention interventions that can support families and communities in raising healthy and well-functioning OBD in the earliest stages and *before* the emergence of clinically significant symptoms of a mental disorder. Presently, however, the availability of preventative treatments with established efficacy for the OBD remains scarce. Indeed, the benefits of psychotropic treatment for reducing prodromal mood symptoms in youth at risk for BD are inconclusive (see McNamara, Nandagopal, Strakowski, & DelBello, 2010 for a review), while efficacy has only been established for one indicated prevention program to date. Specifically, Miklowitz and colleagues have created an adapted version of Family-Focused Therapy for the OBD (FFT; Goldstein & Miklowitz, 1995), consisting of 12 family-based sessions devoted to psycho-education, communication enhancement training, and acquisition of problem-solving skills. The adapted version (FFT-HR) aims to optimize developmental trajectories and clinical course in primarily adolescent (ages 9 to 17 years) and symptomatic (i.e., already exhibiting active mood symptoms) samples of OBD.

The results from one open trial (Miklowitz et al., 2006), one developmental trial (Miklowitz et al., 2011), and three randomized controlled trials (Miklowitz et al., 2008; 2013; 2014) are promising, showing a significant delay in onset of BD or mitigated clinical course of depression one to two years post-intervention. To our knowledge, there are currently no other established psycho-social prevention programs that specifically focus on improving mental health outcomes for the OBD in childhood prior to the emergence of serious mood symptoms.

**Prevention of mental disorders in the offspring of parents with major depression**

Similar to the OBD, the offspring of parents with major depressive disorder (MDD) are at elevated risk for adverse outcomes throughout their lifespan, including a two-to fourfold increase in internalizing and externalizing disorders (e.g., Weissman et al., 2006). Contrary to the OBD, however, a number of selective prevention interventions occurring in groups of adolescents, with families, and within community settings (e.g., in schools) have been conducted with this population (see Beardslee, Gladstone, & O'Connor, 2011; Gladstone & Beardslee, 2009 for reviews).

Data from seven randomized control trials (RCTs) investigating the efficacy of five different selective prevention programs targeting the offspring of parents with MDD was recently assessed in a meta-analysis conducted by Loechner and colleagues (2017). Relative to any control condition (i.e., usual care, waiting list, or active control group), selective prevention programs for the offspring of parents with MDD led to a reduction in rates of internalizing symptoms as well as in the incidence of clinical depression immediately (i.e., up to four months) following intervention, with effect sizes ranging from small to moderate. Conversely, pre-to-post group differences in internalizing symptoms were no longer significant at short-term (five to 12 months) or long-term (15-72 months) follow-up, suggesting that intervention gains generally failed to be maintained over time. Given the recurrent nature of MDD, the authors speculated that offspring's repeated exposure to parental episodes of depression may account for the observed lack of longevity in intervention effects. In fact, parents' depression status at baseline (i.e., whether or not a parent met diagnostic criteria for major depression at enrollment) has been shown to moderate the extent to which families benefit from intervention, with the absence of active depression at baseline predicting greater sustainability of favorable intervention outcomes over time (Beardslee et al., 2013; Brent et al., 2015; Garber et al., 2009; Weersing et al., 2016). Similarly, Weersing and colleagues (2016) reported superior intervention effects in families

where offspring endorsed lower levels of emotional problems and better overall functioning at enrollment, indicating that prevention efforts may be optimally timed during periods of relative wellness in high-risk families. Offspring age and sex, and parental education have also been investigated as possible moderating factors of intervention effects, but have yet to produce any consistent or meaningful patterns of results (Compas et al., 2015). In the end, only a handful of studies thus far have explored moderation within the context of prevention in the offspring of parents with MDD. Even though the literature on prevention intervention is inarguably more developed for this population compared to the OBD, the number of RCTs remains too small for moderation to be evaluated at the meta-analytic level (Loechner et al., 2017).

**Key principles of effective prevention programs**

Knowledge of the key, general principles that underlie effective prevention of mental disorders in youth can assist practitioners in creating comparable programs for the OBD and that are likely to yield the most favorable outcomes. While further research is needed to identify moderating and mediating factors of intervention effects in high-risk children and adolescents, there exists a number of systematic and meta-analytic reviews of the literature on mental illness prevention that have sought to describe the characteristics of successful programs for the prevention of both depression (e.g., Gladstone & Beardslee, 2009; Horowitz & Garber, 2006; Stice, Shaw, Bohon, Marti, & Rohde, 2009) and other mental health problems (e.g., Greenberg, Domitrovich, & Bumbarger, 2001; Nation et al., 2003; Weissberg, Kumpfer, & Seligman, 2003) in community and high-risk samples. These reviews have determined, for example, that prevention programs that specifically target at-risk youth, that is, selective and indicated intervention programs, consistently yield more positive outcomes relative to universal prevention programs. Likewise, multimodal programs that aim to foster a broad range of adaptive skills in replacement of youth problematic behaviors and target more than one proximal (e.g., parental practices), rather than distal (e.g., media), risk or protective factor have been described as most beneficial. Other factors that distinguish between successful and unsuccessful prevention programs include timing and dosing an intervention such that it occurs when it will have maximal impact on a child's developmental trajectory and provides sufficient time to learn, internalize, and practice new skills (typically via a minimum of nine weekly sessions), disseminating an intervention via properly trained and supervised staff, administering homework, and using interactive, research-driven, and developmentally appropriate teaching methods. Ultimately,

reviews of the literature on prevention interventions suggest that incorporation of the aforementioned principles is key to the design and selection of programs that can successfully delay or curtail the development of depressive symptoms and other mental health problems in children and adolescents. These principles may, in turn, serve as a guide for the creation of successful prevention programs that expressly target the OBD.

**Conclusions from the literature on prevention**

Having a parent with BD is associated with a broad range of mental health issues that come at substantial cost to children, families, and societies. As such, prevention programs that aim to reduce risk of maladaptive outcomes in the OBD prior to the emergence of significant clinical symptoms has become an increasingly important endeavour. At present, much more is known about the successful prevention of depression in at-risk youth. Comparatively, prevention efforts directed at the OBD have lagged behind, with efficacy having been established for only one indicated prevention program targeting the OBD in the early stages of an affective disorder. To our knowledge, no selective prevention program targeting unaffected OBD and their families exists.

**Rationale and goals of the current study**

The two primary objectives of this dissertation are to 1) describe parenting practices and parent-child interaction quality as key aspects of the childrearing environment within which the OBD are raised and that contribute to their experience of internalizing and externalizing problems, and 2) establish preliminary efficacy for a selective prevention program aimed at improving the early caregiving environment and mental health of the OBD.

More specifically, in **Chapter 2** (study 1), we sought to characterize the key parenting practices (i.e., levels of structure, control, and support) to which the OBD are exposed during the developmental period of middle childhood. Importantly, we also examined if parenting practices in middle childhood underlay the pathway from having a parent with BD and offspring's experience of internalizing and externalizing symptoms in both middle childhood as well as up to 12 years later, in late adolescence and early adulthood. Given the bi-directional nature of the relations that link the quality of the caregiving environment to mental health in the OBD, controlled longitudinal designs are essential in identifying the direction of effect and elucidating on possible causative relations. In turn, greater knowledge of causal mechanisms would contribute to the development of a comprehensive model explaining the transmission of risk for

mood disorders from one generation of a family to the next. The sample examined in this first study was originally recruited between 1996 and 1998 as part of a longitudinal cohort comprised of both families with and without a parent having a diagnosis of BD, and during which time the offspring were aged between 4 and 14 years. From 2006 to 2010, when the offspring were between 14 and 28 years of age, a two-wave re-assessment was undertaken during which the adolescent and adult offspring were invited to the laboratory to undergo clinical interviews and other research protocols.

In **Chapter 3** (study 2), we evaluate the efficacy of the Reducing Unwanted Stress in the Home (RUSH) program, aimed at ameliorating stressful and chaotic home environments in families with a parent having BD. The RUSH program is a novel approach to prevention intervention in the OBD that has been designed in conjunction with the aforementioned principles of effective prevention programs, as well as research into the individual and environmental risk factors that propagate maladaptive development among the OBD. Through 12 weekly group sessions run separately, but in parallel, for parents with BD and their offspring (aged 6 to 11 years), the RUSH program aims to improve mental health among the OBD by instilling positive changes within the general caregiving environment and strengthening individual stress-coping skills. For the purposes of study 2, parent-child interaction quality, as measured via a laboratory-based paradigm, represented the aspect of the caregiving environment that was of empirical interest. Therefore, the goals were to evaluate parent-child interaction quality in families having a parent with BD prior to and following participation in the RUSH program, and to investigate parent-child interaction quality as a possible mediator of the relation between participating in the RUSH program and offspring's experience of emotional and behavioral problems six months later. Piloting of the RUSH program is still in its early stages, with 26 families with a parent having BD having participated in the full program between 2014 and 2016. The current study was designed as a proof-of-concept trial of the RUSH program, where parent-child interaction quality and mental health symptoms in the OBD were compared to a sample of age-matched ONAD who underwent identical assessments in the laboratory, but did not participate in the RUSH program. While RCTs are considered the "gold standard" for evaluating program efficacy, the low prevalence of parents with BD having young children, and the resulting small sample size, would have rendered a RCT underpowered (e.g., Keen, Pile, & Hill, 2005). Nonetheless, study 2 contributes to the establishment of efficacy for the RUSH

program such that larger (multi-site), RCTs of the RUSH program may be conducted in the future and, eventually, disseminated via mental health practitioners in the community.

# Chapter 2: Parenting practices in middle childhood mediate the relation between growing up with a parent having bipolar disorder and offspring psychopathology from childhood into early adulthood

**Abstract**

The offspring of parents with bipolar disorder (OBD) are at high risk for developing mental disorders. In addition to genetic factors, environmental risk is purported to be associated with these negative outcomes. However, few studies have examined this relation. Using concurrent and longitudinal data, we examined if support, structure, and control provided by parents in middle childhood mediated the relation between having a parent with or without bipolar disorder, and offspring mental health. The sample included 145 offspring (77 OBD; 68 controls) aged 4 to 14 years and their parents. Parent and teacher ratings of child behavior were collected, and diagnostic assessments were conducted in offspring 12 years later (n=101). Bootstrapping analyses showed that low levels of structure mediated the relation between having a parent with bipolar disorder and elevated internalizing and externalizing difficulties during middle childhood. For the longitudinal outcomes, parental control emerged as the strongest mediator of the relation between parents' bipolar disorder and offspring psychopathology. Suboptimal childrearing may have different immediate and enduring consequences on mental health outcomes in the OBD. Parental structure has robust effects on emotional and behavioral problems in middle childhood, while levels of control promote psychological adjustment in the OBD as they mature.

## Introduction

Bipolar disorder (BD) is a chronic and debilitating psychiatric illness. It is among the top ten leading causes of disability worldwide (World Health Organization, 2001), by virtue of its association with severe psychosocial dysfunction, suicidality, and high comorbidity (Hodgins, Faucher, Zarac & Ellenbogen, 2002; Schaffer, Cairney, Cheung, Veldhuizen & Levitt, 2006). As such, it entails important societal and economic costs (Begley, et al., 2001; Das Gupta & Guest, 2002), including particularly heavy burdens for the offspring of parents with BD (OBD). There is substantial evidence of adjustment and mental health problems among the OBD. The OBD display rates of attention, disruptive behavioral, and anxiety disorders in childhood two to nine times those observed among children with healthy parents (Birmaher et al., 2009; Singh et al., 2007). Recent clinical staging models suggest that the OBD are likely to exhibit age-specific emotional and behavioral difficulties prior to the development of sub-clinical affective symptoms and later major affective disorders (Duffy et al., 2010; 2014; 2017; 2018). By young adulthood, approximately 30- 50% of the OBD will have developed a major affective disorder compared with only 10% of the offspring of parents with no affective disorder (ONAD; Mesman, Nolen, Reichart, Wals, & Hillegers, 2013; Nijjar, Ellenbogen, & Hodgins, 2014; Rasic, Hajek, Alda, & Uher, 2013).

Adverse outcomes for the OBD likely stem from a complex interaction between inherited traits and exposure to suboptimal childrearing environments (Brietzke et al., 2012). Genetic predisposition is the primary vulnerability factor reported in twin and adoption studies, with heritability estimates ranging between 79% and 93% (Kieseppa, Partonen, Haukka, Kaprio, & Lonnqvist, 2014; McGuffin et al., 2003). Additionally, since genetic risk does not entirely account for the inter-generational transmission of BD, growing up with a parent who periodically becomes psychotic, dysfunctional, neglectful, or abusive has also been described as a dominant influence on the development of the OBD (Alloy et al., 2005; Post, Leverich, Xing, & Weiss, 2001). In fact, disruptions in caregiving in families in which one parent has BD are well-documented, as indicated by high levels of marital discord and separation (Dore & Romans, 2001; Lam, Donaldson, Brown, & Malliaris, 2005), parental absenteeism (e.g., due to hospitalizations; Pini et al., 2005), non-optimal parenting (e.g., use of lax disciplinary techniques; Calam, Jones, Sanders, Dempsey, & Sadhnani, 2012), and negative communication styles (Inoff-Germain, Nottelmann, & Radke-Yarrow, 1992; Meyer et al., 2006; Vance, Huntley, Espie,

Bentall, & Tai, 2008). With regards to general family dynamics, Chang and colleagues (2001) found that lower levels of cohesion and organization, and elevated conflict characterized families in which one or both parents had BD relative to normative population means. Similar findings have been reported comparing the environment of families with and without a parent with BD (e.g., Barron et al., 2014; Ferreira et al., 2013; Romero, Delbello, Soutullo, Stanford, & Strakowski, 2005).

Dysfunctional caregiving environments in childhood are well-established risk factors for a broad array of mental disorders across the lifespan (see Yap, Pilkington, Ryan, & Jorm, 2014; Yap & Jorm, 2015 for meta-analyses). Within the literature on affectively ill parents, there is robust evidence that unipolar depression in a parent contributes to illness onset in children at genetic risk via an impaired caregiving environment. A recent systematic review conducted by Beardslee, Gladstone, & O'Connor (2011) highlights parenting behaviors including disengagement, low responsiveness, unpredictability, high expressed emotion, and hostility as mechanisms of the parent-child transmission of psychopathology, as is the presence of an insecure parent-child attachment relationship. Among parents with BD, negative bi-directional correlations have been described between the quality of the childrearing environment and the experience of emotional and behavioral problems in the OBD (Calam et al., 2012; Ferreira et al., 2013; Freed et al., 2015). However, only one cross-sectional study to date has examined and found a small, but statistically significant indirect pathway from parent BD to offspring's current BD via heightened levels of family conflict (Schudlich, Youngstrom, Calabrese, & Findling, 2008).

The offspring of parents with BD may be especially susceptible to levels of stress, chaos, and instability in the home. For instance, relative to control offspring, the OBD tend to experience more frequent and severe stressful life events (Ostiguy et al., 2009). Among those who eventually develop a mental disorder, negative life events often precede onset (Hillegers et al., 2004; Wals et al., 2005). High levels of the trait neuroticism - a tendency to react with elevated emotionality to stressors – in parents with BD have also been postulated to elicit unstable and disorganized caregiving environments in middle childhood that increases the risk for later high risk sexual behaviors and poor interpersonal functioning in the OBD (Ellenbogen & Hodgins, 2004; Nijjar, Ellenbogen, & Hodgins, 2016; Ostiguy, Ellenbogen, & Hodgins, 2012). Likewise, structure provided by parents in middle childhood has been shown to

influence cortisol reactivity in adolescence among the OBD (Ellenbogen & Hodgins, 2009; Ellenbogen, Hodgins, & Walker, 2004). In turn, persistent abnormalities in individuals' biological sensitivity to stress have been associated with an increased vulnerability for the development of an affective disorder (Ellenbogen, Hodgins, Linnen, & Ostiguy, 2011; Goodyer, Bacon, Ban, Croudace, & Herbert, 2009). Thus, stability, predictability, and cohesion in the childrearing environment may mediate a variety of health outcomes in youth that have a parent with BD.

Ultimately, the current literature base highlights the need for additional research exploring the causal pathways linking the caregiving environment to mental health outcomes in the OBD. Specifically, longitudinal designs would help determine causality between both factors. It is also possible that disrupted caregiving processes that stem from parental affective disorder convey risk for a variety of maladaptive psychiatric outcomes in youth, and not just for the development of BD. In accordance with clinical staging models of BD, alternative, non-mood disorders should also be investigated as potential adverse outcomes for the OBD. Accordingly, the objectives of the current study were two-fold: 1) to compare the quality of childrearing between families with a parent having BD and control families where neither parent has an affective disorder, and 2) to determine if the quality of the childrearing environment would mediate the relation between offspring's risk status (having a parent with BD versus no affective disorder) and concurrent and prospective internalizing and externalizing symptoms in their offspring. Impairments in the caregiving environment were evaluated across three domains of parenting practices as rated by all parents within a family [i.e., mean levels of support (emotional warmth), structure (i.e., organization and consistency), and control (i.e. disciplinary practices)]. We hypothesized that parents with BD would display non-optimal parenting in all domains relative to control parents. Moreover, we expected that having a parent with BD would increase offspring's likelihood of experiencing emotional and behavioral problems by way of increased disruptions in parenting practices during middle childhood. We explored these patterns at the time 1 assessment, using concurrent measures, and prospectively by examining if parenting practices in middle childhood would continue to mediate the association between offspring risk status (OBD versus offspring of parents with no affective disorder, ONAD) and offspring symptomatology approximately 12 years later as they transitioned into adulthood. In light of previous research showing a greater effect of structure, relative to support and control, provided by parents in middle childhood on

stress reactivity in the adolescent OBD (Ellenbogen & Hodgins, 2009), we postulated that the presence of low structure would yield the strongest predictive relations with symptoms of psychopathology among the OBD relative to the ONAD. Given that there are sex differences in vulnerability to specific internalizing (Angold, Erkanli, Silberg, Eaves, & Costello, 2002) and externalizing (Broidy et al., 2003) pathologies in youth, we also explored whether sex of the offspring moderated the aforementioned statistical associations. To account for the large age-range in the current sample (4 to 13 years at time 1), and the fact the quality of family functioning varies with socioeconomic status (SES; Bradley & Corwyn, 2002), age of the offspring and family income (used as a proxy of SES) were controlled for in all analyses. In order to account for the continuity of mental health problems, issues of bi-directionality and the possibility of evocative effects in the parent-child relationship (Larsson, Viding, Rijsdijk, & Plomin, 2008), psychiatric diagnoses in offspring in middle childhood were controlled for in the mediation analyses. Parents' antisocial personality traits were also included as a covariate to control for the possibility of genetically or environmentally transmitted effects involving parents' antisocial behavior (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005). To the best of our knowledge, this is the first study to evaluate the mediating role of parenting practices on both concurrent and longitudinal mental health outcomes in the OBD.

## Method

### Participants

Participants were recruited for a longitudinal investigation comparing the development of the OBD with that of the ONAD. Parents with a diagnosis of BD were recruited from psychiatric outpatient clinics in the province of Québec, as well as from advocacy and support groups. Control families, where neither parent had a lifetime diagnosis of a major affective disorder nor any current axis-1 diagnosis, were recruited from the same geographic locations via physicians' offices and community organizations. Parental diagnoses were confirmed by an experienced clinician using The Structured Clinical Interview for DSM-III-R (SCID-I; Spitzer, Williams, Gibbon, & Michael, 1992) and from an examination of psychiatric records. The Structured Clinical Interview for DSM-III-R Axis-II personality disorders (SCID-II; Spitzer et al., 1992) was also administered to assess symptoms of antisocial personality disorder in parents. For inclusion, families were required to be fluent in French or English, and have at least one biological child between the ages of 4 and 14 years that had been raised and educated in Canada.

Families in which either parents or children presented with a chronic physical condition, physical handicap, or intelligence quotient (IQ) below 70 were excluded from the study.

Assessments were made at two time points, approximately 12 years apart (11.7 ± 1.0; range 10-14). The initial sample was recruited between 1996 and 1998, and included 145 (76 female) offspring between the ages of 4 and 13 years (*M*=7.89; *SD*=2.41) from 103 families (58 OBD, 45 ONAD). Parents in this sample were mostly Caucasian, middle-class, and French Canadian. Detailed demographic and psychosocial information on the original sample is described in Ellenbogen & Hodgins (2004). One hundred and one (52 female) offspring between the ages of 15 and 21 years (*M*=19.71; *SD*=2.50) from 74 families (42 OBD, 32 ONAD) returned for assessment at least ten years later, consisting of 70% of the original sample. Twenty-nine offspring (19 OBD, 10 ONAD) met DSM-IV (American Psychiatric Association, 1994) criteria for a current diagnosis, including an affective disorder (2 OBD, 0 ONAD), anxiety disorder (15 OBD, 9 ONAD), substance use disorder (6 OBD; 2 ONAD), and four other diagnoses (1 OBD with hypochondriasis, 1 OBD with ADHD, 1 OBD with conduct disorder, and 1 ONAD with Tourette syndrome). No differences were observed between the original sample and those who dropped out 12 years later with regards to offspring problem behavior and IQ, as well as parents' scores across three dimensions of parenting (all $p > .05$).

**Measures**

*Time 1-offspring aged 4-13 years*

Parents completed the Parenting Dimensions Inventory (PDI; Slater & Power, 1987) as a measure of levels of 1) support (i.e., parental warmth, nurturance, and emotional expressiveness; "My child and I have warm, close moments together"), 2) structure (i.e., organization, consistency, predictability; "Once I decide how to deal with a misbehavior of my child, I follow through on it"), and 3) control (i.e., frequency and type of disciplinary strategies; "I do not allow my child to get angry with me") in the home. Parents endorsed items on a scale ranging from one (*not at all characteristic of me*) to six (*very characteristic of me*). Scores for each subscale of the PDI were mean ratings across all parents within a family. In the current sample, the PDI showed adequate internal consistency ($a = 0.80$).

The Achenbach System of Empirically Based Assessment (ASEBA; Achenbach & Rescorla, 2001) is designed to assess children's internalizing and externalizing difficulties across eight dimensions of functioning at home and in school. For the purposes of this study, both the

parent-reported Child Behavior Checklist (CBCL) and Teacher Report Form (TRF) were administered. Composite scores were derived from three subscales (i.e., anxious/depressed, withdrawn/depressed, and somatic complaints) and two subscales (i.e., rule-breaking behavior and aggressive behavior) to assess internalizing and externalizing symptoms in youth, respectively. CBCL scores were averaged across all parents. The TRF was obtained for a subsample of children ($n$ = 105; 55 OBD, 50 controls). Sample items from the internalizing and externalizing composites of the CBCL and TRF include "would rather be alone than with others" and "physically attacks people", which informants endorsed with a 0 (*not true*), 1 (*sometimes true*), or 2 (*very true*). The ASEBA shows adequate test-retest reliability ($k$ = 0.64 – 0.95) and high internal consistencies ($a$ = 0.90) (Achenbach & Rescorla, 2001). Concurrent validity has also been established between the CBCL and other parent-reported behavior scales and diagnostic interviews for children (Barkley, 1998).

The Child Assessment Schedule (CAS; Hodges, Kline, Fitch, Mcknew, & Cytryn, 1981; Hodges, Mcknew, Cytryn, Stern, & Kline, 1982) is a semi-structured, diagnostic interview that was used by trained clinicians to assess for the number of psychiatric symptoms in offspring based on DSM-III (American Psychiatric Association, 1980) criteria. A total score representing the number of current symptoms that met the threshold for clinical significance across all affective, anxious, and disruptive behavior disorders was created. Only parent-reported symptoms were used for the purposes of this study. There is substantial evidence of inter-rater reliability and internal consistency for the CAS (Hodges et al., 1981; 1982). Diagnostic agreement between child and parent informants has also been established (Verhulst, Althaus, & Berden, 1987).

*Time 2-offspring aged 15-21 years*

The Structured Clinical Interview for DSM-IV-R (SCID-I; First, Spitzer, Gibbon, & Williams, 2002) and Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL; Kaufman & Schweder, 2004) were used to assess for the number of current (past month) symptoms of mental disorders in adult and adolescent offspring, respectively. Interviews were conducted by experienced clinicians trained and supervised in the use of the official French and English versions of the SCID-I or K-SADS. In the present study, outcome at the follow-up was defined by the number of symptoms of major depressive disorder, anxiety disorders (generalized anxiety disorder, obsessive-compulsive disorder, social and specific phobia, and post-traumatic stress disorder), and substance use disorders recorded. Given

the low diagnosis rate in the current sample (see participant description above), the number of symptoms reaching the subthreshold or threshold for clinical significance was tallied for each category. Both diagnostic instruments demonstrate adequate psychometric properties (Basco et al., 2000; First et al., 2002; Kaufman et al., 2004). Inter-rater reliability obtained for 15% of interviews in the current sample was excellent ($k$ = .82).

**Procedure**

Following a telephone screening, parents with BD were administered the SCID-I and SCID-II interviews in the laboratory or at their homes, as well as a number of questionnaires. Parents with BD were euthymic during testing. Current spouses and ex-partners were also contacted and requested to complete the same interviews and questionnaires. Next, each parent independently completed the PDI and CBCL, and one parent from each family underwent the CAS interview for each of their children. Lastly, parents provided consent and contact information for their child's teacher to complete the TRF. Control parents underwent the same procedures as families with a parent having BD.

Approximately 12 years later, parents were approached by telephone to provide consent for their adolescent and adult offspring to be contacted by study personnel. Offspring were then scheduled to return to the laboratory to undergo a diagnostic assessment, complete a battery of questionnaires (Nijjar et al., 2014) and information processing tasks, as well as partake in three days of saliva collection in their natural environment (Ostiguy, Ellenbogen, Walker, Walker, & Hodgins, 2011). Only the diagnostic data is used in the present manuscript. Informed written consent was obtained from parents at time 1 and from both parents and offspring at time 2. Offspring participants received an honorarium of $150 CAN at time 2 for participating in the full data collection. All procedures at time 1 and 2 were approved by the Ethics Committee of the Université de Montréal and the Human Research Ethics Committee of Concordia University (Montréal, Canada), respectively.

**Data analysis**

Prior to conducting the analyses, data were screened and corrected for outliers and distributional anomalies that violated statistical assumptions. Cases with missing data at time 2 were deleted listwise. Comparison of the OBD and ONAD on study variables are presented in Table 1.

A Multivariate Analysis of Covariance (MANCOVA) was first conducted to examine differences in the caregiving environment of the OBD relative to the ONAD in middle childhood across mean levels of parents' support, structure, and control, controlling for offspring age and SES. Multivariate significance was determined using Wilk's lambda. A statistically significant multivariate effect was followed-up by three tests of univariate ANCOVA conducted on each dependent variable.

Two overarching, parallel multiple mediation models guided the main analytical procedure for this study, as represented in Figure 1. Parallel multiple mediation models the effects of a predictor on an outcome variable through two or more mediators. The output yields specific indirect effects for each mediator variable included in the statistical model, controlling for their intercorrelations. Hayes (2013) provides a SPSS macro (PROCESS version 2.15) that calculates total (path c; strength of the relation between a predictor and outcome variable prior to accounting for the mediator effects), direct (path $c^1$; strength of the relation between a predictor and outcome variable accounting for the mediator effects), and indirect (path ab; strength of each mediating pathway) effects, as well as describes the relation between the predictor and mediator variables (path a), and the mediator and outcome variables (path b). PROCESS conducts tests of significance by constructing 95% bias-corrected confidence intervals (CI). If the CI does not include zero, the indirect effect is considered statistically significant at the .05 level. For this study, the bootstrap sample was set at 5000 iterations. Lastly, the output also yields partially standardized effect sizes ($C_{ps}$) for the indirect effects, which represents the number of standard deviations by which the dependent variable is expected to increase or decrease per a change in the mediator equal to the size of path a.

For all mediation analyses, the following covariates, all measured at time 1, were included: offspring age, family income, offspring psychiatric diagnoses on the CAS, and parents' antisocial traits as defined by the mean number of SCID-II threshold and sub-threshold symptoms of antisocial personality disorder. To protect against violations of the assumption of independent observations, analyses were conducted with and without siblings (using random deletion). As the mediation analyses yielded similar findings, all participants were included in the final analyses. Lastly, to determine if the mediated associations varied with offspring sex, the above-mentioned analyses were repeated using moderated mediation. However, offspring sex did

not moderate any of the cross-sectional or longitudinal mediated analyses, and was dropped from the final statistical plan (data not shown).

## Results

### Group comparison of parenting practices in middle childhood

Mean levels of parent-rated support, structure, and control in middle childhood were compared between the BD and control families. After controlling for between-group differences in SES and offspring age, a MANCOVA revealed a main effect of group for parenting practices ($F_{(4,138)=}$ 1167.76, $p$ = .000). Post-hoc analyses indicated significantly lower levels of support ($t_{(143)=}$ -3.76, $p$ = .00, $d$ = .63), structure ($t_{(143)=}$ -3.28, $p$ = .00, $d$ = .55), and control ($t_{(143)=}$ -2.12, $p$ = .04, $d$ = .36) in BD relative to control families (see Table 1 for means and standard deviations).

### Mediation of the relation between offspring risk status and internalizing and externalizing problems in middle childhood

Pearson correlations between independent and dependent variables are shown in Table 2. Coefficients of the associations between predictor and mediator variables (paths a in Figure 1), and mediator and outcome variables (paths b in Figure 1) are summarized in Table 3. Coefficients for total, direct, and indirect effects (paths c, $c^1$, and ab in Figure 1) are presented in Tables 4 and 5 for the cross-sectional and longitudinal mediation analyses, respectively. Results for the indirect effects are highlighted in the text below, as a significant indirect effect is exclusively needed to establish mediation (Rucker, Preacher, Tormala, & Petty, 2011).

Mean levels of support, structure, and control provided by parents in middle childhood were tested as potential parallel mediators of the relation between offspring risk status (OBD or ONAD) and parents' report of internalizing and externalizing symptoms on the CBCL. Of the three mediators, structure showed a significant indirect effect of the relation between offspring risk status and rates of internalizing (ab = .97, SE = .56, 95% CI [.15, 2.4]; $C_{ps}$ = .11) and externalizing (ab = 1.31, SE = .64, 95% CI [.38, 2.88]; $C_{ps}$ = .13) symptoms. Weaker, but statistically significant indirect effects on externalizing symptoms were detected for support (ab = .71, SE = .47, 95% CI [.01, 2.0], $C_{ps}$ = .07) and control (ab = -.76, SE = .48, 95% CI [-1.99, -.03], $C_{ps}$ = -.08; see Table 4). Similar to parent-report, significant indirect effects of structure were detected when predicting the level of teacher-reported internalizing (ab = 1.16, SE = .73, 95% CI [.11, 3.12]; $C_{ps}$ = .11) and externalizing (ab = 1.1, SE = .68, 95% CI [.10, 2.95]; $C_{ps}$ = .13) symptoms on the TRF, as well as the total number of clinician-rated symptoms on the CAS (ab =

.52, SE = .32, 95% CI [.06, 1.38]; $C_{ps}$ = .09; see Table 4). In sum, having a parent with BD was associated with lower levels of structure in middle childhood that, in turn, predicted higher rates of parent-reported, teacher-reported, and clinician-rated internalizing and externalizing symptoms in the OBD. A similar pattern of results described the relation between levels of support and parent-reported externalizing symptoms in middle childhood. Conversely, high levels of control were associated with higher rates of parent-reported externalizing symptoms in middle childhood (see Table 3). With the exception of parent-report externalizing symptoms, the indirect effects of support and control were non-significant (all 95% CI contained zero) across all cross-sectional analyses.

**Mediation of the relation between offspring risk status and internalizing and externalizing problems in early adolescence and young adulthood**

Mean levels of support, structure, and control provided by parents in middle childhood were tested as potential parallel mediators of the relation between offspring risk status and current symptoms of depressive, anxiety, and substance use disorders in late adolescence and early adulthood on the SCID-1 or K-SADS. Of the three mediators, control in middle childhood mediated the association between offspring risk status and the number of symptoms of depressive (ab = .16, SE = .09, 95% CI [.02, .43]; $C_{ps}$ = .14) and substance use (ab = .70, SE = .36, 95% CI [.19, 1.67]; $C_{ps}$ = .24) disorders 12 years later. Although weaker than for control, the indirect effect of structure on present symptoms of depression was also statistically significant (ab = -.17, SE = .09, 95% CI [-.44, -.04]; $C_{ps}$ = -.03; see Table 5). Similar to the cross-sectional analyses of parenting and offspring symptoms in middle childhood, low levels of control in middle childhood predicted higher rates of offspring depressive and substance use symptoms in late adolescence and young adulthood. Conversely, high levels of structure in middle childhood were associated with higher rates of depressive symptoms (see Table 3). Across all remaining longitudinal analyses, the indirect effects of structure and support were non-significant (all 95% CI contained zero).

## Discussion

The present prospective study showed that parenting practices in middle childhood mediated the associations between having a parent with or without BD, and internalizing and externalizing symptoms in offspring in middle childhood and approximately 12 years later. As expected, parents with BD displayed significant impairments in parenting practices relative to

control parents, providing less support, structure, and control to their offspring in middle childhood. This is consistent with previous studies of parenting by adults with an affective disorder (Alloy, Abramson, Smith, Gibb, & Neeren, 2006; Dix & Meunier, 2009; Wilson & Durbin, 2010). During middle childhood, parental structure, to a greater extent than support or control, underlay the relation between parents' diagnosis of BD and a range of internalizing and externalizing difficulties in their offspring. Specifically, parents with BD were more likely than their psychologically healthy counterparts to provide low levels of organization, consistency, and stability in the home during middle childhood that, in turn, predicted higher rates of psychopathology in the OBD. These associations remained significant for parent-report, teacher-report, and clinician ratings of offspring psychopathology. In contrast, parental control in middle childhood emerged as the strongest predictor of offspring psychopathology in late adolescence and young adulthood. That is, parents' inability to ensure adequate supervision and role boundaries, as well as set appropriate expectations, limits, and consequences for child misbehavior during middle childhood, mediated the association between having a parent with BD and symptoms of substance use and depressive disorders approximately 12 years later.

The results of the mediation analyses are consistent with the view that poor parenting practices in families that include a parent with BD represent a putative causal mechanism for internalizing and externalizing problems in the OBD (Alloy et al., 2005; 2006; Ellenbogen & Hodgins, 2004). The present findings extend previous findings from this sample. We showed that levels of neuroticism were elevated among parents with BD and associated with a range of non-optimal parenting practices including low warmth, low autonomy support, and ineffective behavioral control, as well as a less organized and consistent parenting style (Ellenbogen & Hodgins, 2004). Parents' traits of neuroticism and agreeableness were robust predictors of internalizing and externalizing problems among their offspring in middle childhood (Nijjar et al., 2016; Ostiguy et al., 2012). These externalizing problems, in turn, place the OBD on trajectories leading to a variety of difficulties in adolescence and young adulthood, such as poor interpersonal functioning and high-risk sexual behaviors. Further, we found that the OBD were more sensitive to the deleterious effects of their parents' neuroticism and its associated environmental consequences than the ONAD (Nijjar et al., 2016; Ostiguy et al., 2012), further highlighting the important role of the home environment in promoting and preventing negative outcomes among the OBD.

Interestingly, the type of parenting practice that was an important predictor of behavioral outcomes differed depending on whether the outcome of interest was assessed concurrently in middle childhood or 12 years later when offspring were in late adolescence and young adulthood. There is evidence that a child's susceptibility to specific disruptions in caregiving depends on their age at exposure (Frick, Christian, & Wootton, 1999). Parenting practices that offer an organized, predictable, and consistent framework for daily living have been primarily associated with enhanced psychological well-being and psychosocial development among younger children. For instance, the use of child and family routines provide a buffer against hyperactivity, impulsivity, and non-compliance in low income, ethnic minority children (Lanza & Drabick, 2011), and internalizing problems in school-aged children (Bridley & Jordan, 2012), as well as predict fewer comorbid emotional and behavioral problems in pre-adolescent youth with attention deficit/hyperactivity disorder (Harris et al., 2013). Likewise, home environments characterized by high levels of disorganization, chaos, and noise have been associated with a range of internalizing, externalizing, and attention problems in preschool and school-aged children (Coldwell, Pike, & Dunn, 2006; Deater-Deckard et al., 2009). Among adolescent populations, low levels of parental behavioral control, including inadequate regulation, monitoring, and supervision of adolescent activities, have been repeatedly linked to increased delinquency and engagement in high-risk behaviors (DeVore & Ginsburg, 2005; Hoeve et al., 2009), greater internalizing problems and steeper trajectories towards externalizing difficulties (Galambos, Barker, & Almeida, 2003), as well as higher rates of antisocial behaviors and depression (Bacchini, Miranda, & Affuso, 2011). Longitudinal associations have also been described between insufficient parental monitoring in early adolescence and increased sexual involvement (Roche, Ahmed, & Blum, 2008), substance use (Findlay, Garner, & Kohen, 2013), and truancy (Stanton et al., 2002) in later adolescence.

In the present study, while a caregiving environment low in parental structure had an immediate impact on the OBD's mental health, the adverse psychological effects of insufficient parental control during middle childhood remained latent until the OBD reached late adolescence and early adulthood. The enduring effects of repeated exposure to suboptimal caregiving environments on offspring's psychological well-being have been well documented (e.g., Hoeve et al., 2009; Morgan, Brugha, Fryers, & Stewart-Brown, 2012; Weich, Patterson, Shaw, & Stewart-Brown, 2009). The current data extend previous findings by suggesting that the impact of early

negative caregiving not only persists, but may also not be apparent, until much later in the course of offspring development. Alternatively, it is possible that the longitudinal findings reflect consistency in parenting practices from childhood into late adolescence. Although not measured in current study, parenting philosophies and practices tend to persist over time (Carrasco, Rodriguez, Del Barrio, & Holgado, 2011; Else-Quest, Clark, & Tresch Owen, 2011). This may be especially characteristic of the child rearing practices adopted by parents with BD, as behavioral and cognitive rigidity is a feature common to many psychopathologies (Schultz & Searleman, 2002). Thus, the OBD who were exposed to low levels of parental control in middle childhood may have continued to experience inadequate parental control as they transitioned into late adolescence and early adulthood that, in turn, contributed to the development of substance use and depressive symptoms.

Although parents with BD provided less support to their offspring than control parents, parental support in middle childhood did not emerge as a central pathway through which BD in a parent led to offspring internalizing and externalizing symptoms in either middle childhood or late adolescence and early adulthood. The finding that parental support failed to independently contribute to internalizing problems in the OBD was especially unexpected, as low parental warmth has been repeatedly associated with depression and anxiety among both general and high-risk pediatric populations (see McLeod, Weisz, & Wood, 2007; McLeod, Wood, & Weisz, 2007 for meta-analyses). This pattern of findings suggests that the OBD may be more susceptible to the adverse effects of disrupted parental structure and control than support. For example, when compared to the ONAD, the OBD display dysregulations in the functioning of the hypothalamic-pituitary-adrenal (HPA) axis, a neuroendocrine system responsible for the secretion of cortisol in response to environmental stressors (Ostiguy et al., 2011). In turn, HPA axis dysfunction may represent a biological marker of vulnerability to psychopathology in the OBD (Ellenbogen et al., 2011) that, in one study, was strongly predicted by disruptions in predictable and consistent caregiving ten years earlier, but not supportive parenting (Ellenbogen & Hodgins, 2009). Thus, the robust effects of parenting structure, rather than support, on mental health in the OBD highlights how the impact of different parenting factors on risk for mental illness may be partly determined by the nature of the vulnerabilities inherent to the population of high-risk youth being studied.

Likewise, parenting practices in middle childhood did not predict symptoms of anxiety in late adolescence and early adulthood, despite anxiety being the most common psychiatric disorder developed by the OBD. This is in line with the findings from a recent systematic review (Wood, McLeod, Sigman, Hwang, & Chu, 2003) and meta-analysis (Yap & Jorm, 2015) demonstrating little evidence for an association between parenting styles and pediatric anxiety. In fact, McLeod and colleagues (2007) conducted two separate meta-analyses into the role of parenting in determining child and adolescent internalizing difficulties. In aggregate, parenting accounted for less than 4% of the total variance in offspring anxiety relative to 8% with regards to depression. This suggests that factors other than parenting may be especially important to consider in the pathogenesis of pediatric anxiety disorders, which may account for the present null result.

Insufficient parental control is particularly salient in the context of families that include a parent having BD, and may have important implications for models of abnormal development among the OBD. Externalizing problems are elevated in the OBD compared to age-matched controls (Klimes-Dougan et al., 2010; Linnen et al., 2009). Moreover, among high-risk offspring who develop BD, there is evidence of a sub-group characterized by antisocial behavior during childhood and adolescence who exhibit a more severe course of BD, including more hospitalizations and episodes, and a higher prevalence of psychotic symptoms during manic episodes (Carlson and Weintraub, 1993). Similarly, OBD who exhibit high levels of quarrelsome behavior in their daily social interactions, relative to those with low levels and to the ONAD, show blunted daytime cortisol levels (Ostiguy et al., 2011), a frequent biological correlate of antisocial behavior (Alink et al., 2008). Externalizing problems, therefore, represent a core feature of premorbid risk among the OBD. As such, parenting behaviors, such as effective disciplinary strategies, that decrease externalizing behaviors in childhood, may have beneficial long-term effects for the OBD. Also, the caregiving environment, specifically the relation between parent and child, interacts with specific genetic variants to modify the risk of delinquency (Nilsson et al., 2015) and depression (Comasco, Aslund, Oreland, & Nilsson, 2013).

Unexpectedly, high levels of structure in middle childhood were significantly related to elevated rates of depressive symptoms in offspring 12 years later. Although a small statistical effect relative to the other reported findings, the direction of the mediating effect was contrary to the cross-sectional results, where high levels of structure were associated with fewer symptoms.

Within community samples, a lack of age-appropriate autonomy granting and enmeshed family interactions have been associated with increased risk for adolescent depression (Jewell & Stark, 2003; Noom, Dekovic, & Meeus, 1999; Yap et al., 2014), both of which could conceivably be a consequence of excessive parental structuring in later developmental stages. In the current study, this finding may be best understood within the context of co-occurring low levels of parental control, which also significantly predicted elevated symptoms of depression 12 years later. Namely, the establishment of rules, schedules, and order in the absence of parental monitoring, limit setting, and consequences may have created erratic, ambiguous, and confusing environments that further contributed to depressive symptomology in the OBD. Possible interpretations remain limited, however, as there are few studies to guide our understanding of how high parental structure might have a unique impact within the context of growing up with a parent with BD and a heightened familial risk for adolescent depression. Additional research is needed of combinations of the different aspects of parenting and outcomes for the OBD.

**Strengths and limitations**

To the best of our knowledge, this is the first study to investigate the mediating role of parenting practices on the mental health outcomes of the OBD in late adolescence and early adulthood, approximately 12 years after the measure of parenting. Thus, these data increase understanding of a putative mechanism that may be causally related to externalizing and internalizing symptoms among the OBD. Offspring psychopathology was independently rated by parents, teachers, and experienced clinicians. Three dimensions of parenting practices were examined simultaneously, allowing for comparisons of relative strength in predicting outcomes in the OBD. Another strength of the study was the estimations of associations of parenting and psychopathology in late adolescence and early adulthood while statistically controlling for offspring psychopathology in middle childhood. This reduced the likelihood that symptoms of depression and substance use disorders in late adolescence and early adulthood simply represented continuity from internalizing and externalizing problems observed in middle childhood, further supporting our finding of the enduring association between parenting practices and offspring psychopathology.

A number of study limitations should be considered when interpreting the results. Parenting practices were only measured when offspring were in middle childhood, limiting knowledge of parenting into late adolescence and early adulthood when the follow-up assessment

of offspring mental health was undertaken. In particular, the absence of parenting measures during adolescence precludes the possibility of assessing how changing parenting practices over time may have influenced outcomes. Another limitation is the large age range of the participants. While parenting was measured during the developmental stage that is commonly described as middle childhood, certain practices will have a differential impact on offspring adjustment based on age (Frick et al., 1999). Parenting practices were assessed using a single self-report measure, which could have been influenced by parents' mental health status (De Los Reyes & Kazdin, 2005). However, parents with BD were in a euthymic state when completing the PDI. The use of an average score that represented levels of support, structure, or control across all parents within a family likely further helped reduce bias and error commonly associated with the use of self-report data derived from a single informant (Kroes, Veerman, & De Bruyn, 2003). However, this approach prevented us from gaining a more comprehensive understanding of the ways in which the specific parenting practices adopted by each caregiver may have interacted to determine psychiatric outcomes in the OBD. There is a growing area of research attesting to the differential impact of mothers' and fathers' parenting strategies on offspring clinical outcomes (McKinney & Renk, 2008; Milevsky, Schlechter, Netter, & Keehn, 2007). Studies have also shown that exposure to competent caregiving from at least one parent provides a buffer against emotional maladjustment in adolescents (Simons & Conger, 2007), and fathers' parenting style in infancy can either exacerbate or protect against the long-term adverse effects of impaired maternal caregiving (Mezulis, Hyde, & Clark, 2004). Given the elevated rates of assortative mating among patients with BD (Mathews & Reus, 2001), the implications with regards to parenting competence may be especially disadvantageous for the OBD. The unique contribution of parental support to offspring mental health may have been more apparent if considered in interaction with, rather than simultaneously to, the other components of parenting. For example, an authoritative parenting style, which combines parenting practices designed to optimize levels of both responsiveness (warmth and involvement) and demandingness (control, monitoring, and structuring), has been consistently linked to psychological well-being in youth (Larzelere, Morris, & Harrist, 2013; Piko & Balazs, 2012). Ultimately, the use of both multiple informants and observation to assess parenting practices should be considered in future studies.

## Conclusions

Low levels of structure provided by parents in middle childhood mediated the relation between having a parent with BD and elevated rates of internalizing and externalizing difficulties in the OBD during middle childhood. For the longitudinal outcomes, parental control in middle childhood emerged as the strongest mediator of the relation between having a parent with BD and offspring psychopathology 12 years later, in late adolescence and early adulthood. These findings support the usefulness of parent training prevention programs targeting the caregiving environment to reduce risk of psychopathology in the OBD. Specifically, the present findings emphasize the promotion of parental monitoring and adaptive disciplinary practices as a means of mental illness prevention, but also highlight the importance of addressing issues of predictability, consistency, and organization in the home environment of the OBD. This is consistent with current trends in the treatment of adult and pediatric BD (Miklowitz, 2010). Further dismantling of parenting constructs is needed to help clarify some of the discrepant and unexpected findings that emerged in the current study. More multi-method, longitudinal research in populations at risk for affective disorders would also be of benefit.

Table 1

*Comparison of offspring of parents with bipolar disorder (OBD) and offspring of parents with no affective disorder (ONAD)*

| | OBD | ONAD | |
|---|---|---|---|
| **Time 1 (1996-1998)** | | | |
| N | 77 | 68 | |
| Sex of offspring (female: male) | (37: 40) | (39: 29) | |
| | *M* (*SD*) | *M* (*SD*) | *F* |
| Offspring age | 8.38 (2.46) | 7.34 (2.24) | 6.98** |
| Parenting practices (PDI)[a] | | | |
| Support | 13.98 (1.08) | 14.66 (1.10) | 14.16** |
| Structure | 8.66 (1.21) | 9.21 (.71) | 10.78** |
| Control | 5.40 (.85) | 5.71 (.88) | 4.48* |
| Offspring CBCL symptoms[a, b] | | | |
| Internalizing | 53.28 (8.34) | 47.28 (8.34) | 15.22** |
| Externalizing | 52.82 (10.91) | 44.98 (9.87) | 20.38** |
| Offspring TRF symptoms[b, c] | | | |
| Internalizing | 54.22 (10.91) | 50.24 (9.12) | 4.06* |
| Externalizing | 52.56 (8.59) | 49.06 (7.42) | 4.96* |
| Offspring # of CAS psychiatric symptoms[d,e] | 8.08 (7.13) | 3.75 (3.90) | 17.12** |
| **Time 2 (2006-2008)** | | | |
| N | 53 | 48 | |
| Sex of offspring (female: male) | (24: 29) | (25: 23) | |
| | *M* (*SD*) | *M* (*SD*) | *F* |
| Offspring age | 20.09 (2.56) | 18.88 (2.53) | 5.92* |
| Offspring # of psychiatric symptoms[f,g] | | | |
| Depressive | .47 (1.15) | .17 (.64) | 2.53 |
| Anxiety | 2.02 (2.77) | 1.40 (2.47) | 1.42 |
| Substance use | 1.72 (3.54) | .52 (1.90) | 4.33* |

*Note.* PDI = Parenting Dimensions Inventory; CBCL = Child Behavior Checklist; TRF = Teacher Report Form; CAS = Child Assessment Schedule.

[a] Represents a mean score across all parents within a family. [b] Represents a t-score. [c] $n = 55$ OBD, 50 controls. [d] From the CAS parent interview. [e] Includes clinical symptoms across all affective, anxious, and disruptive behavior disorders. [f] From the Structured Clinical Interview for DSM-IV or Kiddie Schedule for Affective Disorders and Schizophrenia. [g] Includes present (past month) subclinical and clinical symptoms for each disorder.

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

Table 2

*Pearson correlation coefficients for study variables*

| **Variable** | **1.** | **2.** | **3.** | **4.** | **5.** | **6.** | **7.** | **8.** | **9.** | **10.** | **11.** | **12.** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Offspring risk status | - | -.30** | -.27** | -.17* | .31** | .35** | .20* | .21* | .35** | .13 | .12 | .21* |
| 2. PDI Support | | - | .27** | -.20* | -.19* | -.32** | -.08 | -.12 | -.19* | .03 | .02 | -.10 |
| 3. PDI Structure | | | - | .21** | -.35** | -40** | -.26** | -.29** | -.29** | .19 | -.06 | -.13 |
| 4. PDI Control | | | | - | -.06 | .05 | -.09 | -.05 | -.08 | -.09 | -.10 | -.36** |
| *Offspring outcomes at time 1* | | | | | | | | | | | | |
| 5. CBCL internalizing symptoms | | | | | - | .69** | .49** | .22* | .61** | .03 | .06 | .06 |
| 6. CBCL externalizing symptoms | | | | | | - | .36** | .50** | .60** | .13 | .12 | .19 |
| 7. TRF internalizing symptoms | | | | | | | - | .43** | .33** | -.14 | .09 | .24* |
| 8. TRF externalizing symptoms | | | | | | | | - | .36** | -.06 | .13 | .20 |
| 9. # of CAS psychiatric symptoms | | | | | | | | | - | .18 | .04 | .03 |
| *Offspring outcomes at time 2* | | | | | | | | | | | | |
| 10. # of depressive symptoms | | | | | | | | | | - | .12 | .10 |
| 11. # of anxiety symptoms | | | | | | | | | | | - | .18 |
| 12. # of substance use symptoms | | | | | | | | | | | | - |

*Note.* PDI = Parenting Dimensions Inventory; CBCL = Child Behavior Checklist; TRF = Teacher Report Form; CAS = Child Assessment Schedule.

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

Table 3

*Unstandardized coefficients between independent and mediator variables (paths a), and mediator and dependent variables (paths b) for the cross-sectional and longitudinal mediation models*

| | **Mediator variables** | | |
|---|---|---|---|
| | Support | Structure | Control |
| **Independent[a] → Mediator (paths a)** | | | |
| *For the cross-sectional analyses* | β (SE) | β (SE) | β (SE) |
| Predicting CBCL internalizing symptoms | -.58** (.19) | -.48** (.18) | -.41** (.14) |
| Predicting CBCL externalizing symptoms | -.58** (.19) | -.48** (.18) | -.41** (.14) |
| Predicting TRF internalizing symptoms | -.62* (.24) | -.65** (.22) | -.30 (.18) |
| Predicting TRF externalizing symptoms | -.62* (.24) | -.65** (.22) | -.30 (.18) |
| Predicting # of CAS psychiatric symptoms[b] | -.59** (.19) | -.51** (.18) | -.42** (.14) |
| *For the longitudinal analyses* | | | |
| Predicting # of psychiatric symptoms[c,d] | | | |
| Depression | -.54** (.20) | -.49* (.21) | -.51** (.15) |
| Anxiety | -.55** (.20) | -.49* (.21) | -.50** (.15) |
| Substance Use | -.55** (.20) | -.49* (.21) | -.50** (.15) |
| **Mediator → Dependent (paths b)** | | | |
| *For the cross-sectional analyses* | | | |
| Predicting CBCL internalizing symptoms | -.01 (.73) | -2.00** (.75) | .37 (.94) |
| Predicting CBCL externalizing symptoms | -1.22 (.80) | -2.72** (.82) | 1.82 (1.03) |
| Predicting TRF internalizing symptoms | -.04 (.95) | -1.80 (.99) | -.49 (1.26) |
| Predicting TRF externalizing symptoms | -.12 (.75) | -1.64* (.78) | .39 (.99) |
| Predicting # of CAS psychiatric symptoms[b] | -.57 (.49) | -1.02* (.50) | -.28 (.64) |
| *For the longitudinal analyses* | | | |
| Predicting # of psychiatric symptoms[c,d] | | | |
| Depression | -.03 (.13) | .32** (.12) | -.30 (.17) |
| Anxiety | .30 (.31) | -.05 (.27) | -.00 (.40) |
| Substance Use | -.05 (32) | -.06 (.28) | -1.40** (.42) |

*Note.* CBCL = Child Behavior Checklist; TRF = Teacher Report Form; CAS = Child's Assessment Schedule.

[a] Across all mediation models, the independent variable is offspring risk status (having a parent with BD or not). [b]Includes clinical symptoms across all affective, anxious, and disruptive behavior disorders. [d]From the Structured Clinical Interview for DSM-IV or Kiddie Schedule for Affective Disorders and Schizophrenia. [e] Includes present (past month) subclinical and clinical symptoms for each disorder.

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

Table 4

*Unstandardized coefficients for the total, direct, and indirect effects of offspring risk status on internalizing, externalizing, and total psychiatric symptoms at baseline (cross-sectional analyses) via mean levels of parents' support, structure, and control in middle childhood*

| **Parent Report**[a] | | | | |
|---|---|---|---|---|
| **Effect** | **β** | **SE** | ***p*** | |
| Total | | | | |
| Predicting CBCL internalizing symptoms | 4.06 | 1.51 | .01** | |
| Predicting CBCL externalizing symptoms | 3.39 | 1.66 | .00** | |
| Predicting # of CAS psychiatric symptoms | 3.90 | 1.02 | .00** | |
| Direct | | | | |
| Predicting CBCL internalizing symptoms | 3.23 | 1.62 | .05* | |
| Predicting CBCL externalizing symptoms | 2.37 | 1.78 | .01** | |
| Predicting # of CAS psychiatric symptoms | 2.93 | 1.10 | .01** | |
| Indirect (via mediators) | **β** | **SE** | **95% CI** | **$C_{ps}$** |
| Predicting CBCL internalizing symptoms | | | | |
| Support | .01 | .42 | -.83, .91 | .00 |
| Structure | .97 | .56 | .15, 2.38* | .11 |
| Control | -.15 | .41 | -1.09, .58 | -.02 |
| Predicting CBCL externalizing symptoms | | | | |
| Support | .71 | .47 | .01, 1.98* | .07 |
| Structure | 1.31 | .64 | .38, 2.88* | .13 |
| Control | -.76 | .48 | -1.99, -.03* | -.08 |
| Predicting # of CAS psychiatric symptoms | | | | |
| Support | .34 | .30 | -.13, 1.12 | .06 |
| Structure | .52 | .32 | .06, 1.38* | .09 |
| Control | .12 | .27 | -.30, .83 | .02 |
| **Teacher Report**[b] | | | | |
| **Effect** | **β** | **SE** | ***p*** | |
| Total | | | | |
| Predicting TRF internalizing symptoms | 3.60 | 2.10 | .09 | |
| Predicting TRF externalizing symptoms | 3.39 | 1.66 | .04* | |
| Direct | | | | |
| Predicting TRF internalizing symptoms | 2.27 | 2.27 | .32 | |
| Predicting TRF externalizing symptoms | 2.37 | 1.78 | .19 | |
| Indirect (via mediators) | **β** | **SE** | **95% CI** | **$C_{ps}$** |
| Predicting TRF internalizing symptoms | | | | |
| Support | .03 | .62 | -1.09, 1.43 | .00 |
| Structure | 1.16 | .73 | .11, 3.12* | .11 |
| Control | .15 | .45 | -.47, 1.49 | .01 |
| Predicting TRF externalizing symptoms | | | | |
| Support | .07 | .54 | -.94, 1.29 | .01 |
| Structure | 1.07 | .68 | .10, 2.95* | .13 |

| | | | | |
|---|---|---|---|---|
| Control | -.12 | .38 | -1.25, .40 | -.01 |

*Note*: CBCL = Child Behavior Checklist; CAS = Child Assessment Schedule; TRF = Teacher Report Form; CI = confidence interval; $C_{ps}$ = partially standardized effect size.

[a] $n = 145$; [b] $n = 105$.

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

Table 5

*Unstandardized coefficients for the total, direct, and indirect effects of offspring risk status on symptoms of depressive, anxiety, and substance use disorders*[a,b] *in late adolescence and early adulthood (longitudinal analyses) via mean levels of parents' support, structure, and control in middle childhood*

| **Effect** | **β** | **SE** | ***p*** | |
|---|---|---|---|---|
| Total | | | | |
| Predicting depressive symptoms | .31 | .24 | .21 | |
| Predicting anxiety symptoms | .56 | .53 | .29 | |
| Predicting substance use symptoms | 1.30 | .59 | .03* | |
| Direct | | | | |
| Predicting depressive symptoms | .29 | .27 | .28 | |
| Predicting anxiety symptoms | .70 | .62 | .26 | |
| Predicting substance use symptoms | .29 | .65 | .65 | |
| Indirect (via mediators) | **β** | **SE** | **95% CI** | **$C_{ps}$** |
| Predicting depressive symptoms | | | | |
| Support | .03 | .06 | -.07, .19 | .03 |
| Structure | -.17 | .09 | -.44, -.04* | -.03 |
| Control | .16 | .09 | .02, .43* | .33 |
| Predicting anxiety symptoms | | | | |
| Support | -.17 | .24 | -.75, .25 | -.06 |
| Structure | .03 | .21 | -.33, .55 | .01 |
| Control | .00 | .28 | -.53, .61 | .00 |
| Predicting substance use symptoms | | | | |
| Support | .28 | .24 | -.04, .98 | .09 |
| Structure | .03 | .18 | -.26, .49 | .01 |
| Control | .70 | .36 | .19, 1.67* | .24 |

*Note*: $n = 101$; CI = confidence interval; $C_{ps}$ = partially standardized effect size.

[a] From the Structured Clinical Interview for DSM-IV or Kiddie Schedule for Affective Disorders and Schizophrenia. [b] Includes present (past month) subclinical and clinical symptoms for each disorder.

*$p < .05$.

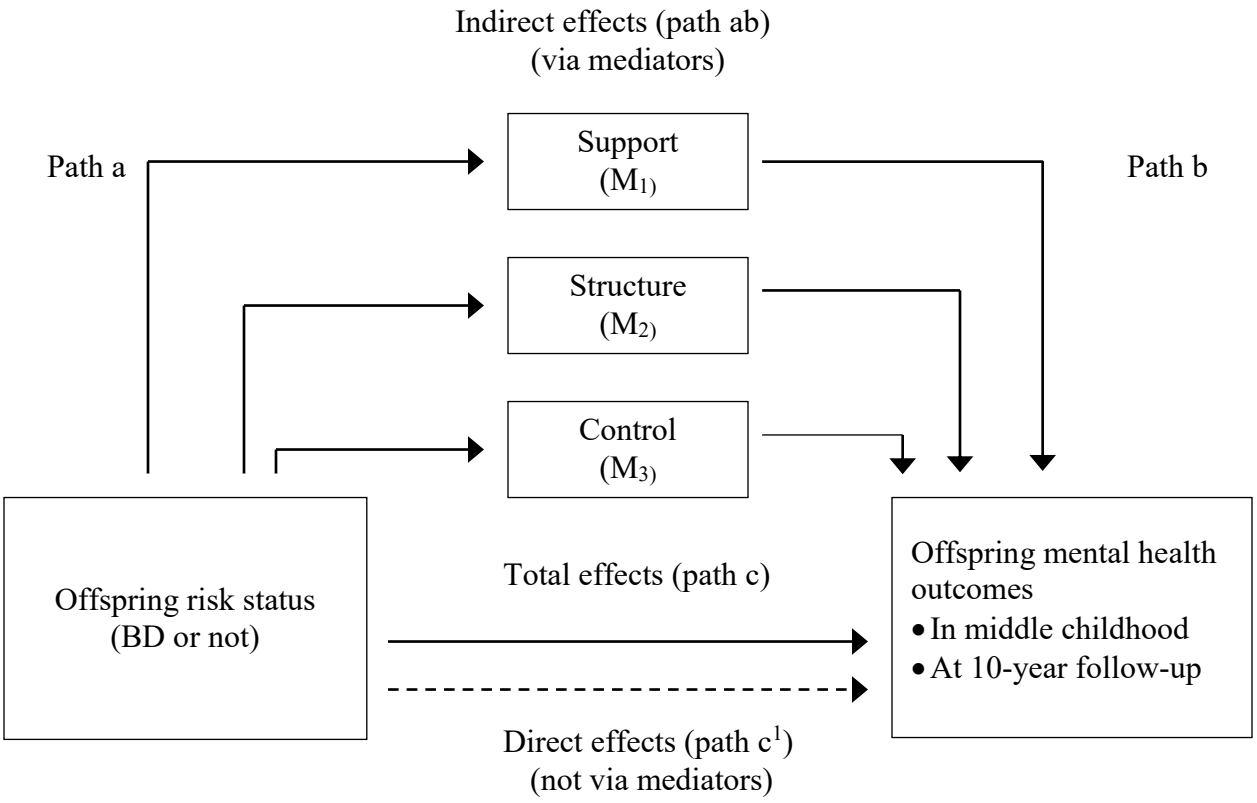


*Figure 1.* Multiple mediation models. Parallel mediators include mean levels of parent-reported support, structure, and control in middle childhood. The cross-sectional model has offspring internalizing, externalizing, and total psychiatric symptoms in middle childhood as the outcomes, respectively. The longitudinal model predicts offspring psychiatric problems ten years later, in late adolescence and early adulthood. BD = bipolar disorder; M = mediator.

## Transition paragraph

Using a controlled longitudinal design spanning approximately 12 years, this first dissertation study demonstrates suboptimal parenting practices within the context of having a parent with BD, as evidenced across low levels of parent-provided support, structure, and control during the developmental period of middle childhood. Nonetheless, it is only low levels of structure and control, relative to support, that emerged as significant mediators of the relation between having a parent with BD and offspring's experience of internalizing and externalizing problems from middle childhood into late adolescence and early adulthood. These data suggest that organization, consistency, and disciplinary strategies used within the childrearing environment during middle childhood are especially important in predicting mental health status in the OBD as they mature, and should be the target of preventative interventions aimed at improving risk trajectories in this population. To our knowledge, this first dissertation study is one of the few to have examined the relations between parenting practices and psychopathology in the OBD - and the first to have established mediation - using a controlled prospective design.

Based on the findings of this first manuscript, and the well-established literature on the etiological factors that perpetuate risk trajectories among the OBD, we created a selective prevention program entitled Reducing Unwanted Stress in the Home (RUSH) aimed at targeting the quality of the childrearing environment in a sample of OBD aged 6 to 11 years with no past or current affective disorders. Preliminary evidence for the RUSH program's efficacy is presented in the second dissertation study. Specifically, we evaluated if participating in the RUSH program would result in positively altered parent-child interaction quality (i.e., levels of parental positivity and negativity, and dyadic mutuality measured during a laboratory-based paradigm) among parents with BD and their biological offspring. We also investigated if pre-to-post changes in parent-child interaction quality would mediate the relation between participating in the RUSH program and the OBD's internalizing and externalizing symptoms six months later. Should participating in the RUSH program lead to reduced rates of emotional and behavioral problems in the OBD by way of post-intervention gains in parent-child interaction quality, findings from study 2 would parallel those yielded in study 1 and provide further support for the possible causal role of childrearing practices in the mental health trajectories of the OBD. Importantly, these data would constitute the first demonstration of efficacy for a selective prevention program designed with the unique needs of the OBD in mind. Study 2 is a proof-of-

concept study, with the primary goal of establishing the efficacy of the RUSH program among the OBD, and contributes to the scarce literature on prevention interventions in the OBD despite the limitation of having used a quasi-experimental design with an assessment-only control group. Although theoretically optimal, the use of a randomized controlled design was precluded by the low prevalence of parents with BD having offspring aged 6-11 years, which would have resulted in a small sample size and underpowered study.

# Chapter 3: Improved parent-child interactions predict reduced internalizing symptoms among the offspring of parents with bipolar disorder undergoing a prevention program: a proof-of-concept study

**Abstract**

The offspring of parents with bipolar disorder (OBD) exhibit elevated rates of psychopathology. However, preventative interventions are lacking. Using a quasi-experimental design with an assessment-only control group, we examined if a 12-week program (entitled Reducing Unwanted Stress in the Home, RUSH) decreases internalizing and externalizing symptoms in the OBD (aged 6-11 years) via intervention-related gains in parent-child interaction quality. Participants initially consisted of 66 offspring (34 OBD; 32 controls) and their parents. Assessments were conducted at four time points up to six months following the end of the RUSH program, during which parent and teacher ratings of child symptoms, and parent-child interaction quality (parental positivity and negativity, and dyadic mutuality) were measured. Multilevel modelling showed improved parental positivity and negativity, and dyadic mutuality among target dyads immediately and six months post-intervention. For the bootstrapping analyses, intervention-related change in parental negativity and positivity mediated the relations between having participated in the RUSH program and lower parent- and teacher-reported internalizing problems among the OBD six months later. These data provide evidence of the efficacy of the RUSH program for OBD who exhibited improved interactions with their parents post-intervention. Further investigation via a randomized controlled trial is warranted.

## Introduction

Children born of parents diagnosed with bipolar disorder (BD), a mood disorder characterized by debilitating episodes of mania and depression, are at risk for a range of adverse negative outcomes throughout their lifespan (Axelson et al., 2015; Mesman, Nolen, Reichart, Wals, & Hillegers, 2013; Nijjar, Hodgins, & Ellenbogen, 2014). Rates of internalizing and externalizing disorders are especially concerning among the offspring of parents with BD (OBD). In childhood, the OBD are more likely to display attention deficit, disruptive, and anxiety disorders than their low-risk counterparts (Birmaher et al., 2009; Singh et al., 2007). In a meta-analytic review (Rasic et al., 2013), approximately 60% of the OBD developed a mental disorder by young adulthood, which included a two- to four-fold increase in the rates of depressive disorders and BD compared to the offspring of parents with no affective disorder. This is consistent with a recent clinical staging model highlighting how early emotional and behavioral problems among the OBD in childhood later transition into sub-clinical depressive symptoms and major mood disorders (Duffy et al., 2010; 2014; 2017; 2018).

In large part, adverse outcomes in the OBD stem from genetic contributions, with twin and adoption studies reporting estimates of heritability ranging between 79% and 93% (Kendler, Pedersen, Neale, & Mathé, 1995; Kieseppä, Partonen, Haukka, Kaprio, & Lonnqvist, 2014; McGuffin et al., 2003). The way in which genetic susceptibility is expressed in the OBD remains unknown, but is likely the consequence of many single nucleotide polymorphisms with small additive effects (e.g., Baum et al., 2008; Ferreira et al., 2008; Sklar et al., 2008). One possibility is that genetic risk is encoded through altered brain structure and function (Whalley et al., 2013) in areas that underlie face emotion processing (Brotman et al., 2008a, 2008b), emotion regulation (Ladouceur et al., 2013), and sensitivity to environmental stress (Ostiguy, Ellenbogen, Walker, Walker, & Hodgins, 2011). Because gene-environment interplay is central in understanding the intergenerational transmission of affective disorders (Rutter, 2009), environmental factors are likely paramount in the development of negative outcomes among the OBD. A key facet of environmental risk is suboptimal childrearing, which has been repeatedly documented in families with a parent having BD. Namely, the OBD tend to grow up in homes characterized by lower levels of cohesion and organization, and elevated conflict compared to low-risk offspring (Barron et al., 2014; Ellenbogen & Hodgins, 2004; Ferreira et al., 2013; Romero, Delbello, Soutullo, Stanford, & Strakowski, 2005). High levels of marital discord and separation (Dore & Romans,

2001; Lam, Donaldson, Brown, & Malliaris, 2005), parental absenteeism (e.g., due to hospitalizations; Pini et al., 2005), non-optimal parenting (e.g., use of lax disciplinary techniques; Calam, Jones, Sanders, Dempsey, & Sadhnani, 2012), and poor parental bonding (Lau et al., 2018) are also evident in families having a parent with BD, and can contribute to symptom onset up to 12 years later (Iacono, Beaulieu, Hodgins, & Ellenbogen, 2017).

In addition to these general features of the family environment, parent-child interactions are widely recognized as an important element of the early caregiving environment by virtue of their role in shaping child development and behavioral patterns across the lifespan (Suldo, 2009). Parents with BD exhibit negative communication styles and affectivity, lack of sensitivity and responsiveness, and increased disengagement, disorganization, tension, and unhappiness when interacting with their offspring compared to parents with no affective disorder (Davenport, Zahn-Waxler, Adland, & Mayfield, 1984; Inoff-Germain, Nottelmann, & Radke-Yarrow, 1992; Radke-Yarrow, Nottelmann, Belmont, & Welsh, 1993; Vance, Huntley, Espie, Bentall, & Tai, 2008). In turn, Meyer and colleagues (2006) linked extreme displays of negative affect and attitudes among mothers with BD during early childhood interactions with their offspring to risk for BD approximately 20 years later. This finding is comparable to earlier, retrospective investigations supporting a positive correlation between dysfunctional parent-child relationships in childhood and adolescence, and adult BD (Alnaes & Torgersen, 1993; Rosenfarb, Becker, & Khan, 1994).

In light of the OBD's susceptibility to psychiatric problems throughout the lifespan, and the elevated societal burden associated with affective disorders (see Ferrari et al., 2013 for a review), preventative interventions are warranted. Family-Focused Therapy (FFT), an adjunct treatment for BD, was modified for use in primarily adolescent youth (aged 9 to 17 years) at high risk for BD, defined as being symptomatic and having a first-degree relative with BD. Through 12 family-based sessions devoted to psycho-education, communication enhancement training, and problem- solving skills, this adapted program strives to reduce risk of syndromal conversion from active mood symptoms to full blown BD. To date, the results from one open trial (Miklowitz et al., 2006), one developmental trial (Miklowitz et al., 2011), and three randomized controlled trials (Miklowitz et al., 2008; 2013; 2014) are promising, demonstrating a significant delay in the onset of BD or mitigated clinical course of depression one to two years post-treatment. Regarding the use of psychotropic treatment for reducing prodromal mood symptoms among youth at risk for BD, the literature remains largely inconclusive (see McNamara,

Nandagopal, Strakowski, & DelBello, 2010 for a review). To our knowledge, no psycho-social prevention efforts have focused on improving mental health outcomes among the OBD in childhood *prior* to the manifestation of clinically significant symptoms of an affective disorder.

To this end, we created a 12-week, skills-based prevention intervention program entitled Reducing Unwanted Stress in the Home (RUSH). The RUSH program aims to prevent the early development of internalizing and externalizing problems among unaffected (i.e., having no mood disorder) OBD during middle childhood (ages 6-11 years) by targeting elevated stress levels, instability, and chaos within the caregiving environment; all of which have been associated with growing up in a family with a parent having BD (e.g., Ellenbogen & Hodgins, 2004). More specifically, the RUSH program teaches parents and their children how to cope with stress, problem-solve, and communicate more effectively, with an additional focus for parents to better manage child behavior and improve organization and consistency in family life. The current research project was designed as a proof-of-concept; mainly, to establish the efficacy of the RUSH program among the OBD using a quasi-experimental design with an assessment-only control group of children being raised by parents with no history of affective disorder (ONAD). Assessments occurred immediately before (T1) and after (T2), as well as three (T3) and six months (T4) following the end of the RUSH program.

For the purposes of this manuscript, the caregiving environment was conceptualized as rater-observed levels of parental negativity (negative affect and control like anger and criticism), parental positivity (positive affect and control like laughter and praise), and dyadic mutuality (coherent, synchronous mutually warm and cooperative interaction) within the parent-child relationship (Deater-Deckard, Pylas, & Petrill, 1997). While a substantial body of literature highlights the adverse outcomes linked to negative parent-child interactions (e.g., see Hoeve et al., 2009; McLeod, Weisz, & Wood, 2007 for meta-analyses), naturalistic home observations reveal that even within distressed families, only one fifth of interactions involve conflict (Gardner, 1987; Reid, 1987). Thus, the remaining positive or neutral interactions likely hold significant influence over the course of child development. Reciprocal dyadic influences are also of growing empirical interest, highlighting the ways in which the thoughts, affects, and actions of the parent and child interlace (Deater-Deckard & O'Connor, 2000; Kochanska, 1997). In childhood, dyadic reciprocity is defined as joint attention, cooperation, shared positive affect, and mutual responsiveness that occurs at the level of the dyad and is qualitatively distinct from

individual displays of positivity. As such, in addition to focusing on the construct of parental negativity, we also chose to investigate positive and dyadic aspects of parent-child interaction in the present study.

The present study had two goals: 1) to determine if the RUSH program elicited immediate (T2) and long-term (T3 and T4) improvements in levels of parental positivity and negativity, and dyadic mutuality during interactions between parents with BD and their offspring, and 2) to explore if positive changes from T1 to T2 within these three components of parent-child interaction mediated the association between having a parent with BD (i.e., having participated in the RUSH program) and offspring's internalizing and externalizing symptoms at T4. Control offspring served as a benchmark from which to compare the OBD's functioning at specific assessment points and estimate pre-to-post-intervention growth among the OBD while controlling for any effects attributable to the passage of time or participating in a research project. We hypothesized that the OBD would display more dysfunctional parent-child interactions than the ONAD at T1. Participating in the RUSH program were expected to yield positive changes within parent-child interaction quality for the OBD, including reduced parental negativity and enhanced parental positivity and dyadic mutuality. We anticipated gains would be apparent immediately (T2) as well as sustained up to six months (T3 and T4) post-intervention. Additionally, we expected that between-group differences in parent-child interaction quality at T1 would dissipate by T4. Lastly, we postulated that having a parent with BD and, thus, having participated in the RUSH program, would decrease offspring's internalizing and externalizing symptoms at T4 by way of positively altered parent-child interaction quality from T1 to T2. Given the dearth of research distinguishing between the effects of negative, positive, and reciprocal parent-child relationships in the OBD, no specific hypotheses were put forth with regards to which of the three components of parent-child interaction would be the strongest mediator of the relation between having participated in the RUSH program and offspring mental health symptoms at T4.

## Method

### Participants

Families with a parent having BD ($n$ = 25) were recruited to participate in a prevention intervention using online and newspaper advertisements, as well as through local clinics and patient support and advocacy groups within the region of Montréal, Quebec. Parental diagnoses

were confirmed by experienced doctoral students in clinical psychology using the Structured Clinical Interview for DSM-IV-R (SCID-I; First, Spitzer, Gibbon, & Williams, 2002). In turn, the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL; Kaufman & Schweder, 2004) was administered to parents to establish their children's past and present mental health status at the start of the study. Senior graduate students were formally trained and supervised on the administration of the SCID-I and K-SADS by the principle investigator. Control families ($n$ = 28), in which neither parent had a lifetime diagnosis of a major affective disorder or any current axis-1 diagnosis, were recruited from the same geographic locations using online and community advertisements. Inclusion criteria included having at least one biological child between the ages of 6-11 years and fluency in English or French. Children who presented with an intellectual or chronic physical disorder, as well as past or present diagnoses of affective, psychotic, or pervasive developmental disorders were excluded from the study. A maximum of two children per family were permitted entry into the study. Offspring from both groups were matched on key demographic variables, including age, sex, ethnicity, and socio-economic status (all $p < .05$). Parents in this sample were mostly Caucasian, middle-class, and French-Canadian. The large majority of families were intact (70%), the rest of parents identifying as single or separated/divorced. Among parents having BD, most (90%) were diagnosed with BD-I. A family physician or psychiatrist followed all parents with BD, and they were being treated with mood stabilizers during the course of the study.

Participants initially consisted of 66 children (34 OBD; 32 ONAD; 48% female) aged 6-11 years ($M$ = 8.2 years; $SD$ = 1.6 years) and a primary caregiver that served as the index parent (primarily mothers). Among the OBD, ten offspring met DSM-IV (American Psychiatric Association, 1994) criteria for a current diagnosis at T1, including an anxiety disorder (1 OBD), enuresis (2 OBD), oppositional defiant disorder (1 OBD), and attention deficit/hyperactivity disorder (6 OBD; all of who were being treated with prescribed psychostimulants). All ONAD were disorder-free at the start of the study. Of the initial 34 OBD who underwent the T1 assessment, 26 completed the RUSH program. Specifically, four families (6 OBD) discontinued participation after the T1 assessment due to scheduling conflicts or lack of time. One family (2 OBD) dropped out of the study midway through the intervention, citing poor fit between their therapeutic needs and the nature of the help offered by the RUSH program. The 26 OBD who completed the RUSH program returned for T2 and T3 assessments, but only 77% of the sample

(20 OBD) was retained at T4. Lack of time was named by families as the most common reason for dropping out at T4. Detailed information regarding attrition rates for the OBD and ONAD is provided in Figure 1.

**Measures**

**Parent-Child Interaction Paradigm (Stevenson-Hinde & Shouldice, 1995; Deater-Deckard & O'Connor, 2000).** Index parents and their offspring were videotaped in the laboratory during a 10-minute, structured cooperation task. During the activity, parent-child dyads were provided with a picture of a house and verbal instructions to replicate the image using an Etch-a-Sketch drawing toy. The Etch-a-Sketch drawing toy is comprised of two control knobs that each produce vertical or horizontal lines, only one of which could be operated by each member of the dyad. Parents interacted separately with each of their children registered in the study and repeated this activity at each of the four assessment phases. To quantify the occurrence of specific parent and child behaviors, two trained research assistants completed eight 7-point Likert-type scales (ranging from low to high in frequency) using the Parent-Child Interaction System (PARCHISY; Deater-Deckard, Pylas, & Petrill, 1997): parental negative (ex. anger) and positive (ex. joy) emotions, parental negative (ex. use of criticism) and positive (ex. use of praise) control, parent responsiveness to child cues and vice-versa (attunement), interactive reciprocity (shared emotional expression), and cooperation. For the purposes of this study, scores obtained on individual scales were averaged to create three composite codes (Atzaba-Poria, Deater-Deckard, & Bell, 2014; Deater-Deckard & Petrill, 2004): 1) parental negativity (parental negative emotions and control), 2) parental positivity (parental positive emotions and control), and dyadic mutuality (co-responsiveness, interactive reciprocity and cooperation). Inter-rater reliability was obtained for 20% of the sample by raters who were blind to offspring group status (OBD v. ONAD) and/or assessment phase (ICC= .81-.90). This is comparable to prior studies employing this measure (e.g., Deater-Deckard, 2000; Klahr, Klump, & Burt, 2015).

**Behavior Assessment System for Children, Second Edition (BASC-2; Reynolds & Kamphaus, 2004).** The BASC-2 is designed to assess children's internalizing and externalizing difficulties across multiple dimensions of functioning at home and in school. The current study utilized scores obtained at T4 from both the Parent Rating Scales (PRS) and Teacher Rating Scales (TRS). Scores were derived from six subscales to assess anxiety, depression, and somatic complaints (internalizing symptoms) as well as hyperactivity, aggression, and conduct problems

(externalizing symptoms) in offspring. The TRS was obtained for a subsample of children (approximately 70%). Sample items from the internalizing and externalizing composites of the PRS and TRS include "cries easily" and "bullies others", respectively, which informants endorsed with a 0 (*never occurs*), 1 (*sometimes occurs*), 2 (*often occurs*), or 3 (*almost always occurs*). The BASC shows adequate test-retest reliability ($k$ = .64 - .95; Merydith, 2001) and high internal consistencies ($a$ = .80 - .90; Tan, 2007). Concurrent validity has also been established with the Achenbach System of Empirically Based Assessment (Achenbach & Rescorla, 2000), another multi-informant behavior scale (Bender, Auciello, Morrison, MacAllister, & Zaroff, 2008).

**Intervention Program: Reducing Unwanted Stress in the Home (RUSH)**

The RUSH program is a 12-session, manual-based prevention intervention program aimed at improving the quality of the caregiving environment while strengthening stress-coping and resilience among the OBD. The program is structured as closed, weekly group sessions that are run separately, but in parallel for parents with BD and their children. Parent sessions are two hours long and follow three core modules devoted to the acquisition and practice of skills related to problem-solving, healthy communication, and organization and discipline in the home. Psycho-education about life stress and adaptive stress-coping is also provided. Child sessions are one hour in duration and focus on teaching individual coping strategies meant to enhance resilience in the face of environmental stress, including thought restructuring, problem-solving, emotion labeling, relaxation, and assertiveness training. Bi-weekly, 15-minute booster calls were arranged with parents, as to provide individualized support and to encourage the use of skills in the home. Make-up sessions, that included a short, but individualized review of missed content, were also offered as needed. Although the RUSH program is a novel approach to mental illness prevention among the OBD, it is based on several previously validated treatments that target stress-coping, family relationships, child-rearing, and the management of bipolar disorder using a cognitive-behavioral approach (Abramowitz, 2012; Kendall & Hedtke, 2006; Miklowitz, 2008; Severe, 2000; Shapiro & Sprague, 2009). A session-by-session breakdown is presented in Table 1.

For the purposes of the current study, intervention groups were created based on availability and initiated on a "rolling basis" for a minimum of five eligible families. Ultimately, five intervention groups were run from May 2014 to June 2016, each comprised of about five to

ten parents or children. Given the well-documented influence of non-specific variables on therapeutic success (Ahn & Wampold, 2001), parents completed in-house questionnaires designed to assess levels of motivation for therapeutic change (at T1) and satisfaction with the RUSH program (at T2) using a 100 point-scale (with higher scores meaning greater motivation or satisfaction). Ratings for both motivation ($M$ = 83.89; $SD$ = 11.09) and satisfaction ($M$ = 88.40; $SD$ = 16.22) were highly positive for the majority of parents in this sample. Likewise, attendance rates were adequate, with most families attending over 10 of the mandated 12 sessions.

Under the supervision of the principle investigator, six senior graduate students in clinical psychology were trained to co-lead group sessions. Sessions were video recorded and later coded by a trained observer with regards to therapist competence and adherence to intervention protocol. A random sample of videos (30%) were coded by a second observer and produced adequate inter-rater reliability (ICC= .89-.98). Coding was largely based on a well-validated scheme developed for cognitive-behavioral group treatments of adults by Hepner, Paddock, Zhou, & Watkins (2011), although slight modifications were made to suit the needs and nature of the RUSH program and the youth group. Therapists' adherence to intervention protocol was generally high (over 90%). Measures of competence were rated using a Likert-type scale ranging from 0 (complete failure to demonstrate the targeted skill) to 6 (skilled and consistent application of the targeted skill) on the following dimensions: levels of warmth/genuineness and empathy, use of guided discovery, ability to collaborate with group members, and the ability to structure and maintain thematic focus during sessions. Overall, the ratings were high across therapists, with average scores ranging from 5.33 to 5.67.

**Procedure**

Following a brief telephone interview, eligible parents were invited to the laboratory to undergo a diagnostic interview (SCID-I) and to report on their child's mental health (K-SADS). Families with a parent meeting diagnostic criteria for BD I/II then took part in the RUSH program. Index parents (80% mothers) and their offspring also completed assessments in the laboratory that included a structured parent-child interaction paradigm and a questionnaire about child emotional and behavioral problems (i.e., parent version of the BASC-2). Parents provided consent and contact information for their child's teacher to complete the teacher version of the BASC-2. Additionally, index parents completed questionnaires relating to general family functioning, parenting stress, and coping. Offspring underwent a battery of neuropsychological

tests as well as cortisol sampling over two days in their natural environment (not reported here). Finally, we conducted an observational assessment of the home environment, via a visit and a short interview (not reported here).

Assessments occurred pre- (T1) and post (T2)-intervention, as well as three (T3) and six (T4) months following the end of the RUSH program. Index parents consisted primarily of the parent having BD, although the healthy spouse served as the index parent for five of the participating 25 families. Nonetheless, all parents within a family were invited to participate in the RUSH program; seven of the 17 intact families had both parents attend over ten of the 12 sessions. Parents with BD were euthymic during testing and there was only one reported instance of a depressive episode during the RUSH program.

Parent-child dyads (86% mothers) from the control group did not participate in the RUSH program, but underwent identical assessments to the OBD according to the same timetable. Participants were remunerated $100 CAN at T1, $80 CAN at T2 and T3, and $100 CAN at T4. Children received small toys as recognition for their participation. Voluntary and informed consent and assent were obtained from the parents and their offspring, respectively. All procedures were approved by the Human Research Ethics Committee at Concordia University Montréal, Canada).

**Data Analysis**

Data were screened for outliers and distributional anomalies that may have violated statistical assumptions. Data for five families (8 OBD) who did not complete any of the post-intervention assessments were deleted listwise. To protect against violations of the assumption of independent observations, analyses were conducted with and without siblings (using random deletion). Likewise, among the OBD, analyses were run to include all dyads or only those comprised of a parent having BD. In both cases, the original results were left unchanged, leading the entire sample to be retained in the final analyses. Because a quasi-experimental design with an assessment-only control group was utilized, offspring risk status (OBD v. ONAD) should be considered synonymous with group membership (i.e., whether or not a family participated in the RUSH program) across all analyses.

**Linear mixed models analyses.** The main efficacy analyses were conducted using a mixed effects model with maximum likelihood (ML) estimation (Heck, Thomas, & Tabata, 2014) with PASW version 22 (IBM, Corp., 2013). In these analyses, individual data points for each

participant were "nested" within the time-related variables. An auto-regressive heterogeneity covariance structure (ARH1) was specified. Offspring age was included as a covariate across all analyses to account for the large age range (6-11 years) in the current sample. Growth trajectories for the OBD and ONAD are visually represented in Figure 2.

The within-subject (level 1) analyses were conducted among the OBD only, with scores for parental negativity, parental positivity, and dyadic mutuality being used as the dependent variables, and the timing of the data collection as the predictor. Six separate models were analyzed for parental negativity, parental positivity, and dyadic mutuality, respectively, examining linear changes immediately post-intervention (from T1 to T2) as well as linear and curvilinear (quadratic and cubic) changes over the following six months (T3 and T4). We also investigated if level 2 factors could explain inter-individual variability in the level 1 effects, including parents' self-reported levels of motivation for therapy at T1 and general satisfaction with the RUSH program at T2, as well as their number of attended group sessions. Ultimately, these variables were removed and the slopes for parental negativity, parental positivity, and dyadic mutuality were set as fixed in the final statistical plan (all $p > .05$; data not shown).

In the between-subject (level 2) analyses, offspring risk status (OBD/intervention v. ONAD/no intervention) was added to account for variability observed in participants' initial status (intercept) and growth trajectories (slope) over time. Because the ONAD did not partake in the RUSH program, their unique growth patterns were not of conceptual interest. As such, only the linear effects of time were tested and used to compare the growth trajectories of the OBD to those of the ONAD. Six separate models were analyzed for parental negativity, parental positivity, and dyadic mutuality, respectively, examining pre-to-post–intervention gains (T1 to T2), and linear growth over the course of the study (T1 to T4). As mother-daughter, mother-son, father-daughter, and father-son relationships may be distinct (Collins & Russell, 1991), sex of the offspring and index parent were also added as predictors in the between-subject analyses.

**Parallel mediation analyses.** Parallel mediation analyses were then conducted to determine if pre-to-post-intervention gains in parental negativity, parental positivity, and dyadic mutuality yielded improvements in offspring's internalizing and externalizing symptoms at T4 (see Figure 3). For each of the three parent-child interaction measures, a change score was calculated by subtracting scores obtained at T2 from those obtained at T1. Little's missing completely at random (MCAR) test (Little, 1988) yielded no evidence that the data were not

MCAR ($p$ = 1.00). Thus, missing data for three families (6 OBD) who completed T3 assessments, but discontinued participation at T4, were handled through multiple imputation for the parent-reported outcomes. However, as these same participants failed to return the teacher version of the BASC-2 at T3 and T4, listwise deletion was used for the teacher-reported outcome data in these three families given the absence of T3 data.

Mediation was assessed via PROCESS version 2.15 (Hayes, 2013), which calculates the strength of the indirect effect for each mediating pathway (path ab) by constructing 95% bias-corrected bootstrap confidence intervals. For this study, the bootstrap sample was set at 5000 iterations. Across all mediation analyses, offspring age and total number of psychological symptoms at T1 (as per parent-report on the BASC-2) were entered as covariates. Because sex differences exist in the prevalence of internalizing (Angold, Erkanli, Silberg, Eaves, & Costello, 2002) and externalizing (Broidy et al., 2003) problems, we also explored if offspring sex moderated the aforementioned statistical associations. As offspring sex was not a significant moderator, it was dropped from the final statistical plan (all $p$ > .05; data not shown). Means and standard deviations for the OBD and ONAD on key study variables at each assessment phase are presented in Table 2.

## Results

### Linear mixed model analyses predicting the OBD's growth trajectories over time

Six, within-subject (level 1) models were assessed among the OBD. Each model included the time-related variables as linear and curvilinear (quadratic, cubic) predictors of change within each of three parent-child interaction measures (i.e., mean scores on parental negativity, parental positivity, or dyadic mutuality) immediately following the end of the RUSH program (T1 to T2) as well as over the course of the study (T1 to T4). Pre-to-post-intervention analyses yielded a significant decrease in parental negativity ($b$ = -.596, $SE$ =. 061, $p$ < .001), and increased parental positivity ($b$ = .250, $SE$ =. 077, $p$ = .001) and dyadic mutuality ($b$ = .115, $SE$ =. 058, $p$ = .048) during interactions between parents with BD and their offspring (i.e., OBD dyads) by T2. When examining growth trajectories over the four time points, a quadratic curve characterized gains in parental positivity for the OBD dyads ($b$ = -.07, $SE$ =. 027, $p$ = .010). Namely, following improvements in parental positivity from T1 to T2, gains made by parents of the OBD stabilized and were relatively sustained until T4. As it pertains to parental negativity ($b$ = -.036, $SE$ =. 008, $p$ < .001) and dyadic mutuality ($b$ = .051, $SE$ =. 009, $p$ < .001), a cubic trajectory best described

fluctuation from T1 to T4. More specifically, the OBD dyads demonstrated a decrease (increase) in parental negativity (dyadic mutuality) from T1 to T2, followed by an increase (decrease) at T3, which was then ameliorated by T4. Thus, intervention effects were attenuated at the T3 assessment for parental negativity and dyadic mutuality, but were improved at the T4 assessment.

**Linear mixed model analyses predicting between-group differences in growth trajectories over time**

Next, between-subject effects (level 2) were examined. Offspring risk status (OBD v. ONAD) was added to the analyses to examine if the RUSH program yielded immediate (from T1 to T2) as well as long-term (T3 and T4) linear changes in parental negativity, parental positivity, and dyadic mutuality among the OBD relative to the ONAD.

**Parental negativity.** There was a significant amount of variability in the intercept for parental negativity at T1 (Wald Z = 3.437, $p$ = .001), meaning that dyads differed in levels of parental negativity at the beginning of the study. Offspring risk status ($b$ = -.002, $SE$ =. 088, $p$ = .985) was not significantly related to average parental negativity at T1. Likewise, the effects for offspring age ($b$ = -.006, $SE$ =. 004, $p$ = .091) and sex ($b$ = .077, $SE$ =. 079, $p$ = .329), and sex of the index parent ($b$ = -.013, $SE$ =. 101, $p$ = .895) were not statistically significant, suggesting that variables other than those included in the present study accounted for between-subject variability in average parental negativity at T1.

Variability in the linear effects of time (Wald Z = 16.078, $p$ < .001) was also statistically significant, indicating that between-subject effects influenced the linear slope of parental negativity across the four measurement occasions. Namely, participation in the RUSH program explained 8.36% of the between-subject variability in the slope for parental negativity, as the OBD dyads showed significantly larger declines in parental negativity than the ONAD dyads both immediately post-intervention ($b$ = -.510, $SE$ =. 073, $p$ > .001) as well as over the course of the study ($b$ = -.170, $SE$ =. 041, $p$ > .001). This suggests that undergoing the RUSH program improved parental negativity in families having a parent with BD over and above natural changes expected with the passage of time and resulting from being enrolled in a research study. Offspring sex was also a significant predictor of the linear effects of time ($b$ = -.094, $SE$ =. 042, $p$ = .027), accounting for an additional 4.68% of the between-subject variability in the slope for parental negativity. Namely, dyads consisting of a male offspring showed larger declines over the course of the study than those comprised of a female offspring. The sex of the index parent was

not a significant predictor of the linear slope for parental negativity ($b$ = -.036, $SE$ =. 053, $p$ = .502).

**Parental positivity.** Similar to parental negativity, there was a significant amount of variability in the intercept for parental positivity at T1 (Wald Z = 9.210, $p$ < .001). Offspring risk status ($b$ = -.029, $SE$ =. 078, $p$ = .716) and sex ($b$ = .066, $SE$ = .073, $p$ = .373) were not significantly related to average parental positivity at T1. Conversely, the effects for offspring age ($b$ = .006, $SE$ =. 002, $p$ < .001) and sex of the index parent ($b$ = .463, $SE$ =. 097, $p$ < .001) were statistically significant and accounted for 2.85% and 3.91%, respectively, of the between-subject variability in the parental positivity intercept. Both older age in the offspring ($M$ = 3.923, $SD$ = .902) and female sex in the parent ($M$ = 3.808, $SD$ = .836) predicted higher levels of parental positivity at T1 compared to younger age ($M$ = 3.620, $SD$ = .749) and being a father ($M$ = 3.563, $SD$ = .825), respectively.

Likewise, variability in the linear effects of time (Wald Z = 22.172, $p$ < .001) was statistically significant. Participation in the RUSH program explained 8.58% of the between-subject variability in the linear slope for parental positivity, with the OBD dyads showing greater gains than the ONAD dyads from T1 to T2 ($b$ = .629, $SE$ = .088, $p$ < .001) as well as over the four measurement occasions ($b$ = .201, $SE$ = .034, $p$ < .001). Unlike parental negativity, offspring sex did not significantly predict the linear slope for parental positivity ($b$ = -.020, $SE$ = .033, $p$ = .547). However, the sex of the index parent significantly influenced the linear effects of time on parental positivity ($b$ = -.127, $SE$ = .044, $p$ = .004), with fathers demonstrating more growth than mothers over time.

**Dyadic mutuality.** There was a significant amount of variability in the intercept for dyadic mutuality (Wald Z = 8.483, $p$ < .001), such that offspring risk status ($b$ = -.243, $SE$ =. 062, $p$ = .002) was significantly related to average dyadic mutuality at T1 and explained 4.34% of the between-subject variability. More specifically, the OBD dyads ($M$ = 2.375, $SD$ = .424) displayed fewer instances of co-responsiveness, interactive reciprocity, and cooperation at T1 than control dyads ($M$ = 3.625, $SD$ = .557). The effects of offspring age ($b$ = .008, $SE$ =. 002, $p$ < .001) and sex of the index parent ($b$ = .749, $SE$ =. 099, $p$ < .001) accounted for an additional 5.00% and 9.55%, respectively, of the between-subject variance in dyadic mutuality at T1. Namely, dyads comprised of an older offspring ($M$ = 3.261, $SD$ = .792) or female parent ($M$ = 3.281, $SD$ = .989) showed greater dyadic mutuality at T1 than those having a younger offspring ($M$ = 2.892, $SD$ =

.791) or male parent ($M$ = 2.625, $SD$ = .664). Offspring sex was not a significant predictor of the intercept for dyadic mutuality ($b$ = -.061, $SE$ =. 075, $p$ = .414).

Again, variability in the linear (Wald Z = 22.179, $p$ < .001) effects of time was statistically significant. Participation in the RUSH program explained 5.52% of the between-subject variability in the linear slope for dyadic mutuality, with the OBD dyads showing greater gains than the ONAD dyads from T1 to T2 ($b$ = .271, $SE$ = .096, $p$ = .005) as well as from T1 to T4 ($b$ = .149, $SE$ = .035, $p$ < .001). In fact, offspring risk status was no longer significantly related to the intercept when set to represent average levels of dyadic mutuality at T4 ($b$ = -.028, $SE$ = .062, $p$ = .647), as both the OBD ($M$ = 3.132, $SD$ = .847) and ONAD ($M$ = 3.086, $SD$ = .757) dyads demonstrated comparable levels of interactive mutuality by the end of the study (see Figure 2, panel C). Offspring sex ($b$ = .109, $SE$ =. 035, $p$ = .001) and the sex of the index parent ($b$ = -.199, $SE$ =. 045, $p$ < .001) were also significant predictors of the linear effects of time, and accounted for an additional 0.66% and 5.74%, respectively, of the between-subject variability in the slope for dyadic mutuality. Namely, dyads consisting of a female offspring or male parent showed higher growth rates than dyads having a male offspring or female parent, respectively.

**Parallel mediation analyses predicting offspring symptomatology at T4 via pre-to-post-intervention gains in parent-child interaction quality**

Coefficients of the associations between predictor and mediator variables (paths a in Figure 3), and mediator and outcome variables (paths b in Figure 3) are summarized in Table 3. Coefficients for total, direct, and indirect effects (paths c, $c^1$, and ab in Figure 3) are presented in Tables 4 and 5 for the parent- and teacher-reports of offspring symptoms, respectively. Results for the indirect effects are highlighted in the text below, as a significant indirect effect is exclusively needed to establish mediation (Rucker, Preacher, Tormala, & Petty, 2011). Because the effects of the RUSH program on parent-child interaction quality were inconsistent at T3 (i.e., following quadratic or cubic trends), the following analyses focus on the study end point, T4, exclusively.

Pre-to-post-intervention gains (T2-T1) in parental negativity and positivity, and dyadic mutuality were tested as potential parallel mediators of the relation between having participated in the RUSH program and levels of internalizing and externalizing symptoms on the BASC-2 at T4. None of the parent-child interaction measures yielded a significant indirect effect for the total number of parent- and teacher-reported internalizing and externalizing symptoms in offspring at

T4 (all $p < .05$; data not shown). As such, the individual problem scales that make up each of the internalizing (anxiety, depression, and somatic complaints) and externalizing (hyperactivity, aggression, and conduct problems) composites of the BASC-2 were used as outcomes in the remaining mediation analyses.

Of the three mediators, parental negativity showed a significant indirect effect of the relation between having participated in the RUSH program and rates of parent-reported anxiety (ab = 1.039, SE = .854, 95% CI [.112, 3.101]; $C_{ps}$ = .198) and somatic (ab = .673, SE = .562, 95% CI [.104, 2.095]; $C_{ps}$ = .199) symptoms. Pre-to-post-intervention change in dyadic mutuality also yielded a significant indirect effect for the number of parent-reported somatic symptoms at T4 (ab = -.186, SE = .207, 95% CI [-.774, -.003]; $C_{ps}$ = .055); although, the effect was less strong than for parental negativity. As it pertains to teacher report, significant indirect effects for parental positivity were observed when predicting the number of anxious (ab = -1.410, SE = .970, 95% CI [-3.485, -0.304]; $C_{ps}$ = .356) and depressive (ab = -1.340, SE = 1.449, 95% CI [-4.509, -0.186]; $C_{ps}$ = .245) symptoms at T4. Across all mediation analyses, participation in the RUSH program was associated with a decrease in parental negativity and increase in parental positivity and dyadic mutuality from T1 to T2 (paths a; see Table 3) that, in turn, predicted lower rates of parent- and teacher-reported internalizing symptoms in the OBD at T4 relative to the ONAD (paths b; see Table 3). None of the parent-child interaction measures yielded a significant indirect effect for rates of hyperactivity, aggression, and conduct problems in offspring at T4 (data is presented in Tables 4 and 5).

## Discussion

The present study investigated changes in the quality of parent-child interactions following participation in a 12-week prevention intervention (RUSH program) targeting stress in the home and the quality of the caregiving environment in the OBD relative to healthy control dyads who completed all assessments, but not the intervention. Three main findings emerged. First, levels of dyadic mutuality were significantly different between the OBD and ONAD pre-intervention, with OBD dyads showing lower levels of dyadic mutuality than controls at T1. Surprisingly, there were no significant group differences between the OBD and ONAD on levels of parental negativity and positivity at T1. Second, participating in the RUSH program resulted in reduced parental negativity and enhanced parental positivity and dyadic mutuality among the OBD dyads immediately post-intervention (T2). These gains remained apparent at the six-month

follow-up assessment (T4). Importantly, the OBD dyads improved to the extent that they no longer differed from controls in levels of dyadic mutuality following participation in the RUSH program. Third, although intervention induced changes in parent-child interaction quality did not alter overall levels of internalizing and externalizing symptoms in the OBD, significant effects were observed for specific types of internalizing problems. That is, pre-to-post-intervention improvements (T2-T1) in parental negativity and positivity mediated the relation between having participated in the RUSH program and lower rates of parent-reported anxiety and somatic symptoms, and teacher-reported anxiety and depressive symptoms, respectively, among the OBD six months later. Although a smaller effect size than the above findings, intervention-related improvements in dyadic mutuality mediated the relation between participating in the RUSH program and lower parent-reported somatic symptoms in the OBD at the six-month follow-up.

Contrary to our initial predictions, intervention-related changes in the quality of parent-child interactions lacked stability, as it was only intervention gains in parental positivity that were sustained throughout the three post-intervention assessment points (from T2 to T4). Post-intervention changes in parental negativity and dyadic mutuality at T2 were also present at the study end point (T4), but following a period of attenuated gains at the three-month follow-up assessment (T3). Lifestyle changes are notoriously difficult to make and maintain. The notion of "lapse", defined as a brief "slip" or temporary return to pre-treatment levels of behavioral patterns (Brownell, Marlatt, Lichtenstein, & Wilson, 1986), is therefore well-known within the clinical literature and generally anticipated in the normal course of treatment (see Hunsley, Elliott, & Therrien, 2013 for a review). It is also conceivable that unlearning an old habit is more difficult than acquiring a new one, which may at least partly explain why changes in parental positivity (e.g., increasing the frequency of smiling and verbal praise) were more stable during the six-month period that followed the RUSH program compared to levels of parental negativity (e.g., refraining from providing harsh criticism) and dyadic mutuality (e.g., replacing an autonomous approach to task completion with a cooperative one).

Certain internalizing, but not externalizing, problems were significantly reduced among the OBD as a result of intervention-related changes in parent-child interaction quality. Although we expected intervention-related changes across all symptoms, these results are consistent with clinical trials showing that Family-Focused Treatment for youth at high risk for BD are especially beneficial for improving symptoms on the internalizing spectrum of mental illness (Goldstein et

al., 2014; Miklowitz et al., 2008; 2013; 2014). One possibility is that the RUSH program, being geared towards the promotion of stress-coping, healthy communication, organization, and problem-solving within the overall caregiving environment, may have been better suited to deal with emotional rather than behavioral problems in the OBD. In fact, the RUSH program features only two parent sessions that explicitly address and teach positive disciplinary techniques and behavioral contingency strategies for the management of youth misbehaviors; a leading treatment for disruptive disorders in children and adolescents (see Steiner, 1997; Steiner & Remsing, 2007 for reviews). Thus, a robust and focused behavioral approach would likely better target externalizing problems in the OBD than RUSH's focus on the caregiving environment.

Interestingly, pre-to-post intervention changes in parental negativity and positivity, relative to dyadic mutuality, were most strongly related to lower rates of parent-reported anxiety and somatic symptoms, and teacher-reported anxiety and depressive symptoms, respectively, at T4. These findings are consistent with a large body of research that links exposure to a negative parental style (i.e., high in hostility, harshness, and rejection) with depression and conduct problems in children and adolescents (Hoeve et al., 2009; McLeod, et al., 2007), and studies showing that the presence of positive parental behaviors (e.g., high in warmth, support, and nurturance) tends to protect against psychological maladjustment in offspring (see Khaleque, 2013 for a meta-analysis). In at-risk community samples, interventions that target negative and positive aspects of parenting and parent-child interaction (e.g., Triple P-Positive Parenting Program; Parent-Child Interaction Therapy) have been shown to reduce aggression, opposition, depression, and anxiety problems in youth (see Carpenter, Puliafico, Kurtz, Pincus, & Comer, 2014; Thomas & Zimmer-Gembeck, 2007 for reviews). As such, the current findings provide important evidence that the RUSH program can similarly lead to positive changes in those key parental behaviors that characterize the ways in which parents with BD interact with their offspring, and subsequently result in reduced rates of certain types of internalizing symptoms among the OBD.

Surprisingly, while levels of dyadic mutuality differed at baseline and were significantly improved following participation in the RUSH program, the relation between pre-to-post intervention change in dyadic mutuality and parent-reported offspring symptoms was weaker than for parental negativity. This finding is contrary to prior community and clinical research linking greater parent-child dyadic mutuality to lower levels of emotional and behavioral

problems in infancy and toddlerhood (see Leclère et al., 2014 for a review), and middle childhood (Deater-Deckard & Petrill, 2004; Deater-Deckard, Atzaba-Poria, & Pike, 2004). However, none of these previous studies investigated the construct of dyadic mutuality in conjunction with other components of parent-child interactions, so it might be the case that parental negativity has stronger effects on the development of at-risk offspring than dyadic mutuality. While speculative, another possibility is that mutuality within the parent-child relationship, relative to parental negativity, may primarily affect wellness factors not measured in the current study (e.g., interpersonal functioning or prosocial behaviors).

Importantly, this is the first prevention intervention study to show evidence of improved emotional symptoms six months post-intervention via positive changes in parent-child interaction quality in a sample of young OBD with no history of affective disorder. Miklowitz and colleagues (e.g., 2008; 2013; 2014) have previously provided empirical support for delayed or mitigated clinical course of depression among the OBD following Family-Focused Therapy for BD in high risk youth. These clinical trials have been conducted primarily on older youth (aged 9 to 17 years) who have prominent symptoms of a major affective disorder, including meeting diagnostic criteria for pediatric BD. In the last few decades, a number of randomized controlled trials (RCTs) have emerged and demonstrated efficacy for seven different prevention intervention programs targeting the offspring of parents with major depressive disorder (see Loechner et al., 2017 for a meta-analysis), another population at risk for affective disorders and other mental health problems throughout the lifespan (e.g., Weissman et al., 2006). The content (i.e., teaching skills based on cognitive-behavioral therapy) and structure (e.g., intervene in parents and offspring using a group format) of these programs are similar to those of the RUSH program. However, these interventions differ from the RUSH program in that the RUSH program focuses on middle childhood, with the explicit intent to intervene in high-risk families prior to their offspring entering adolescence, when the onset of a major affective disorder is elevated (Warner, Weissman, Fendrich, Wickramaratne, & Moreau, 1992). In most other prevention programs (Loechner et al., 2017), the target populations are at-risk adolescents, some of whom have already developed a major affective disorder (e.g., Beardslee et al., 2013; Compas et al., 2009; 2011). Another unique feature of the RUSH program is that it does not address BD per se, but, instead, strives to minimize the adverse impact of certain well-established risk factors (e.g., exposure to stressful and chaotic home environments) for BD and other psychiatric problems in

the OBD. In contrast, most prevention intervention programs focus on psycho-education and coping skills that are directly associated with depressive symptomatology (e.g., Clarke et al., 2001; Compas et al., 2009; 2011; Garber et al., 2009). Thus, the RUSH program builds on an empirical literature of prevention studies for mood disorders in youth, but is novel and unique in its aim to target some key family-related risk factors associated with having a parent with BD.

Although the RUSH program does not directly target children's mental health, anxiety, somatic, and depressive symptoms declined at T4 in children whose parent-child interaction quality improved in response to the intervention. Prevailing hypotheses suggest that susceptibility to psychopathology among the OBD may be the consequence of a gene-environment interaction, which refers to the differential influence that exposure to an environment can have in individuals with different genotypes (Ottman, 1996). The interaction can be expressed in a diathesis-stress framework, which anticipates stronger correlations between genotype (diathesis) and outcome under negative (stressful) relative to positive environmental conditions (Rosenthal, 1963; Zuckerman, 1999). Thus, one possibility is that the RUSH program, by reducing conflict and enhancing organization and limit setting within the home environment, while simultaneously strengthening individual stress coping and resilience, altered developmental processes that stem from the interplay between exposure to suboptimal childrearing environments and the expression of biological markers of risk. These biological markers of risk may include weaker connectivity between cortical and subcortical brain regions involved in emotion regulation (Ladouceur et al., 2013; Singh et al., 2014) or elevated production of the hormone cortisol in response to stressful environments (Ostiguy et al., 2011). Importantly, it could be speculated that by specifically reducing emotional problems during middle childhood, the benefits of the RUSH program on the OBD may persist throughout their development. Indeed, internalizing problems in childhood, such as somatization and anxiety, have been directly associated with the subsequent development of mood disorders (Duffy et al., 2010; 2012) and other maladaptive behaviors (e.g., engagement in high-risk sexual behaviors; Nijjar, Ellenbogen, & Hodgins, 2016) in the OBD. Likewise, the experience of non-specific or subthreshold mood symptoms are considered key clinical predictors for the eventual syndromal transition from depression to full blown BD (Fiedorowicz, Endicott, & Akiskal, 2013). Investigation of the RUSH program via a larger RCT and with a longer post-intervention time frame is needed to directly examine this hypothesis.

Of note, while consensus largely existed between parent and teacher ratings of change in offspring internalizing symptomatology from T1 to T4, the reported improvements were each attributable to post-intervention changes within two different components of parent-child interaction. That is, change in parental negativity led to a decrease in specific internalizing symptoms in the home, but not the school, environment, and vice-versa for parental positivity. Importantly, parent-child interaction quality was observed and rated in the laboratory, indicating that these data cannot be explained by differences across informant reports. There is some evidence to suggest that the presence of an authoritative (i.e., warm affect and sensitivity to child cues; firm, but flexible limit setting) rather than the absence of an authoritarian (i.e., strict and rigid limit setting; use of punishment) parenting style within the home environment is most strongly related to increased achievement motivation, school engagement, and academic performance in youth (e.g., Ginsburg & Bronstein, 1993; Rivers, Mullis, Fortner, & Mullis, 2012; Steinberg, Lamborn, Dornbusch, & Darling, 1992). This may explain, at least in part, why the effects of increased parental positivity, rather than decreased parental negativity, reverberated into the classroom context; an increase in academic engagement, motivation, and interest possibly being perceived by teachers as a decrease in symptoms of anxiety and depression among the OBD.

**Strengths and limitations**

This study provides the first test of efficacy for a prevention program targeting the OBD prior to the emergence of clinically significant symptoms of a major affective disorder. To minimize errors and biases associated with the use of self-report from a single informant presenting with a history of mental illness (De Los Reyes & Kazdin, 2005; Kroes, Veerman, & De Bruyn, 2003), information about offspring psychopathology was gathered from caregivers and teachers, and parent-child interactions were based on observation conducted in the laboratory. Parents with BD were also in a euthymic state when completing assessments. Further, three dimensions of parent-child interaction were examined simultaneously, allowing for comparisons of relative strength in predicting outcomes among the OBD.

Interpretations of the current data are limited by the use of a quasi-experimental design. Specifically, while it was possible to determine that the OBD benefitted from participating in the RUSH program over and above natural changes expected with the passage of time and resulting from being enrolled in a research study, it is not known whether the OBD's intervention-related

progress would exceed those observed in OBD participating in a wait-list control or active control (e.g., psychoeducation) group. Designed as a proof-of-concept, the current findings are nonetheless sufficiently promising as to warrant further investigation of the RUSH program using a RCT design. Dismantling research will also be needed in order to identify the features of the RUSH program that are the active mechanisms of change. A limitation of the study is its small sample size, although the effects of this problem were minimized to some degree by the use of non-parametric statistical procedures. Another limitation is that families recruited for this research project were primarily intact and "middle-class", and showed elevated motivation for participating in the RUSH program. All parents with BD also received regular medical or psychiatric follow-up in their community, and thus demonstrated relatively stable clinical course throughout the duration of this study. It will be important to replicate the current findings using a larger and more diverse sample of families with BD. This may include studying more families in which the father is the parent with BD. Finally, behaviors measured in the laboratory may not be entirely representative of parent-child interactions in the natural environment. Supplementing laboratory-based observation with self-report or observation made within the broader, day-to-day home environment should be considered in future studies.

**Conclusions**

The present findings add to a growing literature showing the caregiving environment as a core determinant of risk for psychopathology among the OBD (Iacono et al., 2017; Lau et al., 2018; Meyer et al., 2006). Specifically, the present study provides preliminary evidence that parent-child interactions can be targeted through a relatively brief and skill-based intervention that decreases anxiety, depression, and somatic symptoms in the OBD up to six months later. This is consistent with the growing popularization of family-based treatments for adult and pediatric BD (see Miklowitz & Chung, 2016 for a review). Ultimately, the current data highlight the need for a broad-based prevention approach to wellness in at-risk families, which is especially relevant to the OBD where the presence of non-specific emotional symptoms in childhood are associated with the development of mood disorders in adulthood (Duffy et al., 2010; 2014). Despite the promise of the present findings, further investigation of the efficacy of the RUSH program using a RCT design is required to determine its usefulness in the OBD and other populations at risk for affective disorders.

Table 1

*Session descriptions for the parent and youth groups of the RUSH program*

| Session # | Brief description |
|---|---|
| **Parent group** | |
| 1 | Orientation to the program and fostering motivation for change |
| 2 | Identification and management of stressors |
| 3 | Problem solving: Individual applications |
| 4 | Problem solving: Family applications |
| 5 | Enhancing communication: Active listening |
| 6 | Enhancing communication: Assertive communication |
| 7 | Enhancing communication: Expressing emotions and needs |
| 8 | Implementing structure and consistency: Time management and organization |
| 9 | Implementing structure and consistency: Family routines and household rules |
| 10 | Implementing structure and consistency: Management of child misbehaviors |
| 11 | Implementing structure and consistency: Management of child misbehaviors |
| 12 | Review and maintenance |
| **Youth group** | |
| 1 | Orientation to the program and fostering motivation for change |
| 2 | Understanding and recognizing stress |
| 3 | Identifying emotions |
| 4 | Expressing emotions to cope with stress |
| 5 | The body's reaction to stress |
| 6 | Breathing techniques to cope with stress |
| 7 | Recognizing thoughts |
| 8 | Modifying negative self-talk to cope with stress |
| 9 | Introduction to problem solving |
| 10 | Using problem solving to cope with stressful situations |
| 11 | Assertive communication |
| 12 | Review and maintenance |

Table 2

*Means and standard deviations (SD) for key study variables across the four time points*

| | T1 | T2 | T3 | T4 |
|---|---|---|---|---|
| **Variable** | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
| Parent-child interaction[a] | | | | |
| Parental negativity | | | | |
| OBD | 1.87 (.67) | 1.27 (.35) | 1.33 (.53) | 1.26 (.35) |
| ONAD | 1.53 (.64) | 1.45 (.59) | 1.76 (.75) | 1.35 (.54) |
| Parental positivity | | | | |
| OBD | 3.62 (.77) | 3.87 (.94) | 3.87 (.87) | 3.76 (.99) |
| ONAD | 4.00 (.73) | 3.62 (.63) | 3.40 (.59) | 3.93 (.95) |
| Dyadic mutuality | | | | |
| OBD | 2.87 (.77) | 2.98 (.70) | 2.77 (.53) | 3.13 (.85) |
| ONAD | 3.36 (.89) | 3.21 (.80) | 2.98 (.76) | 3.09 (.76) |
| Offspring PRS symptoms[b,c] | | | | |
| Internalizing symptoms | | | | |
| OBD | 25.12 (10.01) | 22.78 (12.36) | 23.31 (13.51) | 21.75 (11.35) |
| ONAD | 21.48 (11.14) | 19.10 (10.31) | 19.62 (11.53) | 17.69 (11.03) |
| Anxiety | | | | |
| OBD | 11.50 (5.41) | 11.00 (6.64) | 11.15 (6.75) | 9.95 (5.40) |
| ONAD | 12.48 (6.16) | 11.03 (6.39) | 11.03 (5.82) | 10.38 (6.25) |
| Depression | | | | |
| OBD | 8.65 (4.44) | 7.92 (4.21) | 7.92 (5.11) | 7.20 (3.81) |
| ONAD | 5.83 (3.82) | 5.03 (3.48) | 5.00 (4.14) | 4.41 (3.85) |
| Somatization | | | | |
| OBD | 4.96 (3.17) | 3.85 (3.85) | 4.23 (3.71) | 6.60 (4.02) |
| ONAD | 3.17 (2.75) | 3.03 (2.34) | 3.59 (3.31) | 2.89 (3.23) |
| Externalizing symptoms | | | | |
| OBD | 19.46 (11.69) | 17.58 (11.12) | 17.62 (10.32) | 18.40 (11.25) |
| ONAD | 13.76 (7.74) | 15.28 (8.05) | 14.62 (8.10) | 13.83 (7.80) |
| Hyperactivity | | | | |
| OBD | 9.19 (5.49) | 7.85 (5.55) | 8.04 (4.94) | 7.90 (4.76) |
| ONAD | 6.14 (3.86) | 6.59 (4.76) | 6.21 (4.22) | 5.97 (4.20) |
| Aggression | | | | |
| OBD | 5.31 (4.15) | 5.12 (3.66) | 5.04 (3.36) | 5.05 (3.72) |
| ONAD | 5.38 (2.65) | 5.03 (2.23) | 4.86 (2.46) | 4.66 (2.39) |
| Conduct problems | | | | |
| OBD | 4.96 (3.71) | 4.62 (3.16) | 4.54 (3.26) | 5.45 (3.68) |
| ONAD | 2.62 (2.96) | 3.22 (4.69) | 2.79 (3.95) | 3.07 (2.65) |
| Offspring TRS symptoms[d] | | | | |
| Internalizing symptoms | | | | |
| OBD | 13.52 (11.33) | 11.28 (10.68) | 12.37 (10.36) | 10.29 (10.62) |

| | | | | |
|---|---|---|---|---|
| ONAD | 7.96 (6.87) | 9.23 (7.39) | 10.95 (9.31) | 6.67 (10.10) |
| Anxiety | | | | |
| OBD | 5.90 (4.64) | 4.17 (4.89) | 4.63 (4.62) | 5.07 (4.39) |
| ONAD | 3.81 (3.54) | 3.91 (3.06) | 4.14 (3.85) | 4.00 (3.55) |
| Depression | | | | |
| OBD | 4.67 (4.92) | 4.61 (4.71) | 5.84 (4.67) | 4.21 (4.92) |
| ONAD | 3.04 (3.33) | 3.95 (4.34) | 5.48 (4.78) | 4.00 (5.73) |
| Somatization | | | | |
| OBD | 2.95 (4.38) | 2.50 (2.66) | 2.21 (2.96) | 3.21 (3.91) |
| ONAD | 1.12 (1.75) | 1.36 (2.17) | 1.33 (1.88) | .89 (2.17) |
| Externalizing symptoms | | | | |
| OBD | 13.19 (11.28) | 12.94 (14.39) | 11.11 (13.90) | 14.43(11.71) |
| ONAD | 10.69 (13.10) | 9.64 (8.24) | 9.85 (13.53) | 10.78 (14.39) |
| Hyperactivity | | | | |
| OBD | 7.24 (5.61) | 5.72 (5.49) | 5.68 (6.27) | 7.71 (6.41) |
| ONAD | 5.62 (6.51) | 5.41 (4.81) | 4.95 (6.16) | 5.44 (5.92) |
| Aggression | | | | |
| OBD | 3.33 (3.81) | 4.00 (5.40) | 3.68 (4.92) | 3.64 (3.52) |
| ONAD | 2.54 (3.99) | 2.54 (2.86) | 2.86 (4.11) | 3.22 (4.95) |
| Conduct problems | | | | |
| OBD | 2.62 (2.96) | 3.22 (4.69) | 2.79 (3.95) | 3.07 (2.65) |
| ONAD | 2.54 (3.45) | 1.77 (1.74) | 1.86 (3.45) | 2.11 (4.19) |

*Note.* OBD = offspring of parents with bipolar disorder; ONAD = offspring of parents with no affective disorder; PRS = parent report scale; TRS = teacher report scale; T1 = pre-intervention; T2 = post-intervention; T3 = 3-month follow-up; T4 = 6-month follow-up.

[a] From ratings made during the completion of a laboratory-based, parent-child interaction paradigm using an etch-a-sketch toy. [b] From the Behavior Assessment Schedule for Children (BASC-2). [c] T1 ($n$ = 34 OBD, 32 ONAD), T2 ($n$ = 26 OBD, 29 ONAD), T3 ($n$ = 26 OBD, 29 ONAD), T4 ($n$ = 20 OBD, 29 ONAD). [d] T1 ($n$ = 21 OBD, 26 ONAD), T2 ($n$ = 18 OBD, 22 ONAD), T3 ($n$ = 19 OBD, 20 ONAD), T4 ($n$ = 14 OBD, 18 ONAD).

Table 3

*Unstandardized coefficients between independent and mediator variables (paths a), and mediator and dependent variables (paths b) for mediation analyses*

| | **Mediator variables**[d] | | |
|---|---|---|---|
| | Parental negativity | Parental positivity | Dyadic mutuality |
| | β (SE) | β (SE) | β (SE) |
| **Independent**[a] **→ Mediator (paths a)**[b] | | | |
| For parent-reported symptoms[c] | -.47* (.20) | .49* (.25) | .31 (.28) |
| For teacher-reported symptoms | -.47* (.23) | .48* (.24) | .28 (.38) |
| **Mediator → Dependent (paths b)** | | | |
| *For parent-reported symptoms* | | | |
| Predicting anxiety symptoms | -2.23 (1.24) | -.15 (1.03) | .89 (.92) |
| Predicting depressive symptoms | -.99 (.77) | -.59 (.64) | .02 (.57) |
| Predicting somatic symptoms | -1.44 (.79) | .21 (.65) | -.61 (.59) |
| Predicting hyperactivity symptoms | -.51 (.90) | -.19 (.75) | -1.35* (.67) |
| Predicting aggressive symptoms | .42 (.68) | -.02 (.56) | -.14 (.50) |
| Predicting conduct symptoms | -.21 (.74) | .01 (.61) | -.03 (.55) |
| *For teacher-reported symptoms* | | | |
| Predicting anxiety symptoms | .23 (1.17) | -2.31* (1.13) | 1.23 (.76) |
| Predicting depressive symptoms | 1.94 (1.68) | -2.77 (1.81) | .13 (1.13) |
| Predicting somatic symptoms | .13 (.99) | -.98 (1.07) | .33 (.67) |
| Predicting hyperactivity symptoms | -2.09 (1,74) | -3.09 (1.87) | -.66 (1.17) |
| Predicting aggressive symptoms | .38 (1.38) | -1.46 (1.48) | -.58 (.93) |
| Predicting conduct symptoms | -.42 (1.08) | -2.06 (1.16) | .16 (.73) |

*Note.* [a] Across all mediation analyses, the independent variable is whether or not a family participated in the RUSH program, which should be considered synonymous with offspring risk status (having a parent with BD or not); [b] Values for paths a are the same across all parent- and teacher-reported symptoms, respectively; [c] From the Behavior Assessment Schedule for Children (BASC-2) at T4; [d] Scores represent pre-to-post-intervention change in levels of parental negativity, parental positivity, and dyadic mutuality, as calculated by subtracting T2 scores from those obtained at T1.

*$p < .05$.

Table 4

*Unstandardized coefficients for the total, direct, and indirect effects of offspring risk status on parent-reported internalizing and externalizing symptoms at T4 via pre-to-post-intervention change in parental negativity, parental positivity, and dyadic mutuality (n =55)*

| **Effect** | **β** | **SE** | ***p*** | |
|---|---|---|---|---|
| Total | | | | |
| Predicting anxiety symptoms | -1.61 | 1.61 | .32 | |
| Predicting depressive symptoms | 1.66 | .99 | .10 | |
| Predicting somatic symptoms | 1.01 | 1.04 | .34 | |
| Predicting hyperactivity symptoms | .47 | 1.20 | .69 | |
| Predicting aggressive symptoms | -.34 | .85 | .69 | |
| Predicting conduct symptoms | 1.61 | .91 | .08 | |
| Direct | | | | |
| Predicting anxiety symptoms | -2.85 | 1.80 | .12 | |
| Predicting depressive symptoms | 1.48 | 1.12 | .19 | |
| Predicting somatic symptoms | .41 | 1.14 | .72 | |
| Predicting hyperactivity symptoms | .74 | 1.31 | .57 | |
| Predicting aggressive symptoms | -.09 | .98 | .92 | |
| Predicting conduct symptoms | 1.52 | 1.06 | .16 | |
| Indirect (via mediators) | **β** | **SE** | **95% CI** | **$C_{ps}$** |
| Predicting anxiety symptoms | | | | |
| Parental negativity | 1.04 | .85 | .11, .3.10* | .20 |
| Parental positivity | -.08 | .49 | -1.16, .47 | .01 |
| Dyadic mutuality | .27 | .40 | -.04, 1.41 | .05 |
| Predicting depressive symptoms | | | | |
| Parental negativity | .47 | .52 | -.01, .1.83 | .14 |
| Parental positivity | -.29 | .42 | -1.34, .09 | .09 |
| Dyadic mutuality | .01 | .25 | -.37, .41 | .00 |
| Predicting somatic symptoms | | | | |
| Parental negativity | .67 | .56 | .10, 2.10* | .20 |
| Parental positivity | .11 | .33 | -.37, .66 | .03 |
| Dyadic mutuality | -.19 | .21 | -.77, -.01* | .06 |
| Predicting hyperactivity symptoms | | | | |
| Parental negativity | .24 | .66 | -.47, 1.75 | .06 |
| Parental positivity | -.09 | .53 | -1.37, .37 | .03 |
| Dyadic mutuality | -.42 | .41 | -1.31, .04 | .12 |
| Predicting aggressive symptoms | | | | |
| Parental negativity | -.19 | .51 | -1.12, .50 | .07 |
| Parental positivity | -.01 | .36 | -.79, .35 | .00 |
| Dyadic mutuality | -.04 | .19 | -.50, .12 | .02 |
| Predicting conduct symptoms | | | | |
| Parental negativity | .09 | .49 | -.51, 1.11 | .03 |
| Parental positivity | .00 | .39 | -.86, .41 | .00 |
| Dyadic mutuality | -.01 | .23 | -.43, .27 | .00 |

*Note*. CI = confidence interval; $C_{ps}$ = partially standardized effect size; *$p < .05$.

Table 5

*Unstandardized coefficients for the total, direct, and indirect effects of offspring risk status on teacher-reported internalizing and externalizing symptoms at T4 via pre-to-post-intervention change in parental negativity, parental positivity, and dyadic mutuality (n =32)*

| **Effect** | **β** | **SE** | ***p*** | |
|---|---|---|---|---|
| Total | | | | |
| Predicting anxiety symptoms | 1.09 | 1.47 | .46 | |
| Predicting depressive symptoms | .35 | 2.12 | .87 | |
| Predicting somatic symptoms | 2.13 | 1.19 | .08 | |
| Predicting hyperactivity symptoms | .85 | 2.28 | .71 | |
| Predicting aggressive symptoms | -.25 | 1.69 | .88 | |
| Predicting conduct symptoms | .76 | 1.36 | .58 | |
| Direct | | | | |
| Predicting anxiety symptoms | 2.32 | 1.66 | .17 | |
| Predicting depressive symptoms | 2.55 | 2.38 | .29 | |
| Predicting somatic symptoms | 2.58 | 1.41 | .08 | |
| Predicting hyperactivity symptoms | 1.55 | 2.47 | .53 | |
| Predicting aggressive symptoms | .79 | 1.95 | .69 | |
| Predicting conduct symptoms | 1.51 | 1.53 | .33 | |
| Indirect (via mediators) | **β** | **SE** | **95% CI** | **$C_{ps}$** |
| Predicting anxiety symptoms | | | | |
| Parental negativity | -.09 | .88 | -2.16, .61 | .02 |
| Parental positivity | -1.41 | .97 | -3.48, -.30* | .36 |
| Dyadic mutuality | .28 | .51 | -.23, 1.54 | .07 |
| Predicting depressive symptoms | | | | |
| Parental negativity | -.90 | 1.44 | -4.39, .21 | .16 |
| Parental positivity | -1.34 | 1.45 | -4.51, -.02* | .24 |
| Dyadic mutuality | .04 | .60 | -.47, 1.58 | .01 |
| Predicting somatic symptoms | | | | |
| Parental negativity | -.06 | .62 | -1.29, .61 | .02 |
| Parental positivity | -.47 | .89 | -1.99, .85 | .15 |
| Dyadic mutuality | .09 | .35 | -.19, .98 | .03 |
| Predicting hyperactivity symptoms | | | | |
| Parental negativity | .97 | 1.23 | -.38, 3.42 | .16 |
| Parental positivity | -1.49 | 1.45 | -4.31, .03 | .25 |
| Dyadic mutuality | -.18 | .58 | -1.82, .28 | .03 |
| Predicting aggressive symptoms | | | | |
| Parental negativity | -.18 | .98 | -2.27, .90 | .04 |
| Parental positivity | -.70 | 1.03 | -2.88, .35 | .16 |
| Dyadic mutuality | -.16 | .47 | -1.30, .19 | .04 |
| Predicting conduct symptoms | | | | |
| Parental negativity | .20 | .73 | -.97, 1.23 | .06 |
| Parental positivity | .19 | .64 | -.92, 1.12 | .08 |
| Dyadic mutuality | .05 | .30 | -.19, .91 | .01 |

*Note*. CI = confidence interval; $C_{ps}$ = partially standardized effect size; *$p < .05$.

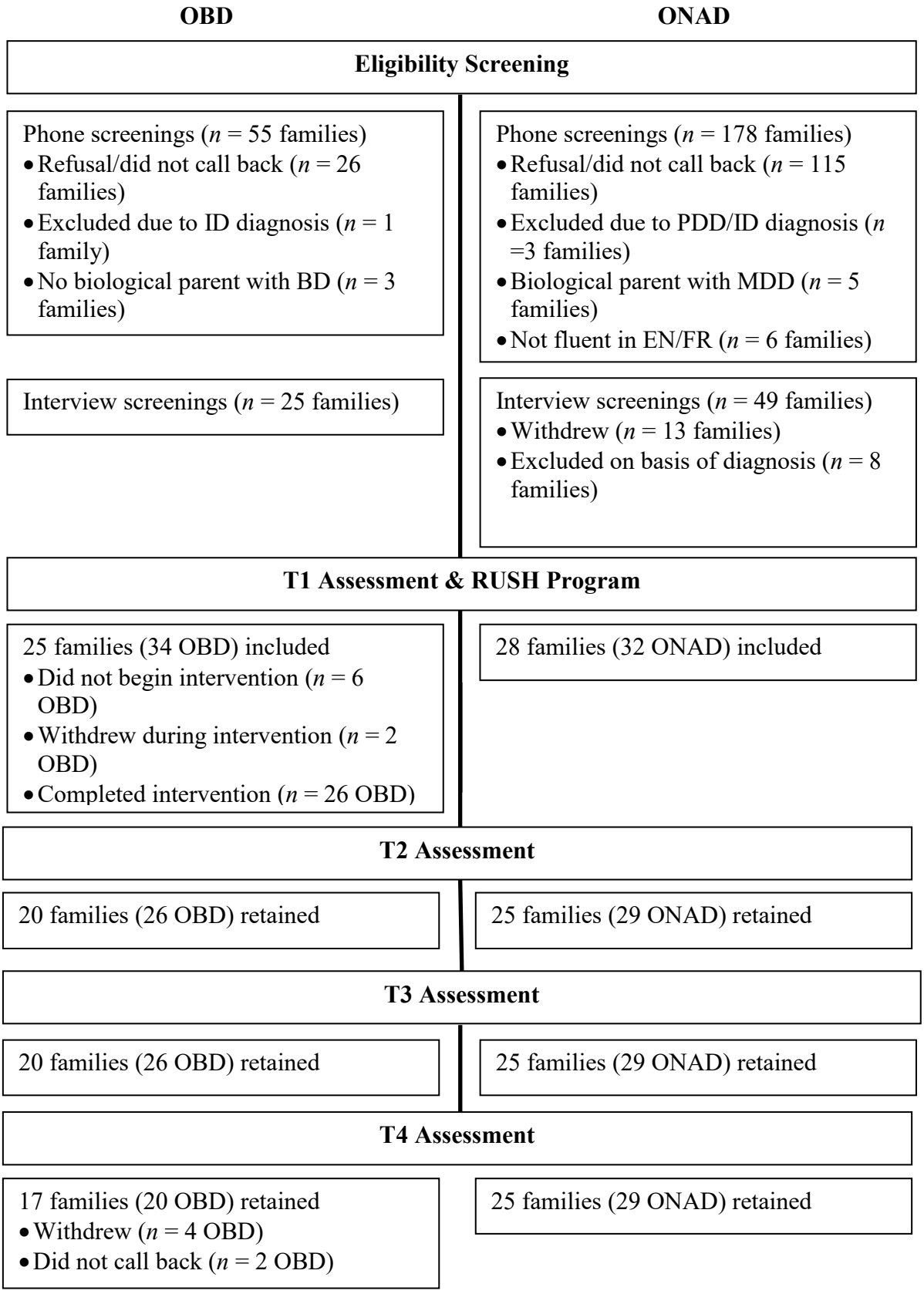
OBD
ONAD
Eligibility Screening
Phone screenings (n = 55 families)
• Refusal/did not call back (n = 26 families)
• Excluded due to ID diagnosis (n = 1 family)
• No biological parent with BD (n = 3 families)
Phone screenings (n = 178 families)
• Refusal/did not call back (n = 115 families)
• Excluded due to PDD/ID diagnosis (n =3 families)
• Biological parent with MDD (n = 5 families)
• Not fluent in EN/FR (n = 6 families)
Interview screenings (n = 25 families)
Interview screenings (n = 49 families)
• Withdrew (n = 13 families)
• Excluded on basis of diagnosis (n = 8 families)
T1 Assessment & RUSH Program
25 families (34 OBD) included
• Did not begin intervention (n = 6 OBD)
• Withdrew during intervention (n = 2 OBD)
• Completed intervention (n = 26 OBD)
28 families (32 ONAD) included
T2 Assessment
20 families (26 OBD) retained
25 families (29 ONAD) retained
T3 Assessment
20 families (26 OBD) retained
25 families (29 ONAD) retained
T4 Assessment
17 families (20 OBD) retained
• Withdrew (n = 4 OBD)
• Did not call back (n = 2 OBD)
25 families (29 ONAD) retained

*Figure 1.* Sample retention by group. OBD = offspring of parents with BD; ONAD = offspring of parents with no affective disorder; BD = bipolar disorder; MDD = major mood disorder; PDD = pervasive developmental disorder; ID = intellectual disability; EN = English; FR = French; T1 = pre-intervention; T2 = post-intervention; T3 = 3-month follow-up; T4 = 6-month follow-up.

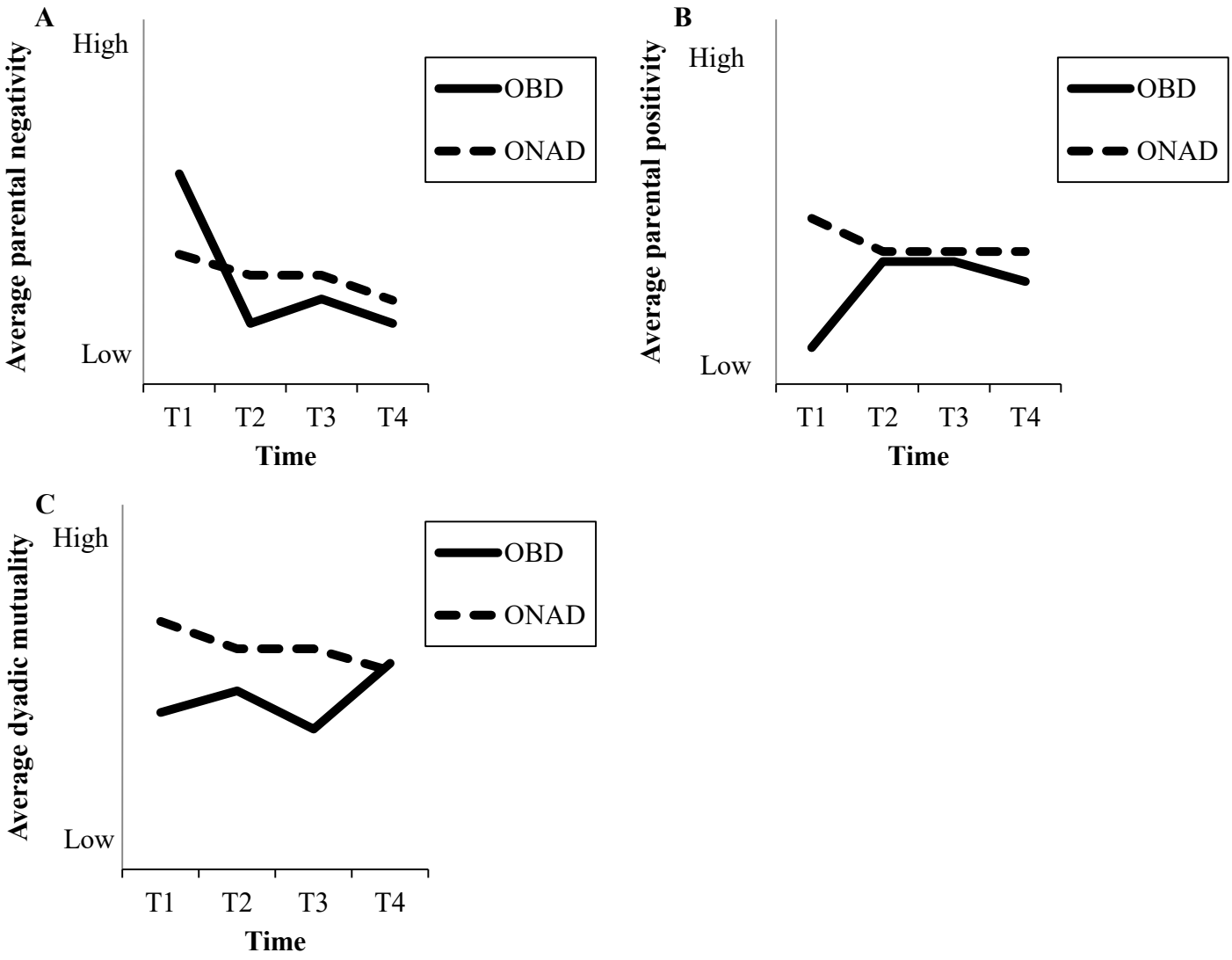


*Figure 2.* Average growth rates in parent-child interaction quality for the OBD and ONAD as measured via laboratory-based observation across the four measurement points. Panels **A** and **C** depict this relation for parental negativity and dyadic mutuality, respectively. In both cases, a cubic trend best describes growth rates from T1 to T4. Panel **B** depicts average growth in parental positivity from T1 to T4 as a quadratic trend. OBD = offspring of parents with bipolar disorder; ONAD = offspring of parents with no affective disorder; T1 = pre-intervention; T2 = post-intervention; T3 = 3-month follow-up; T4 = 6-month follow-up.

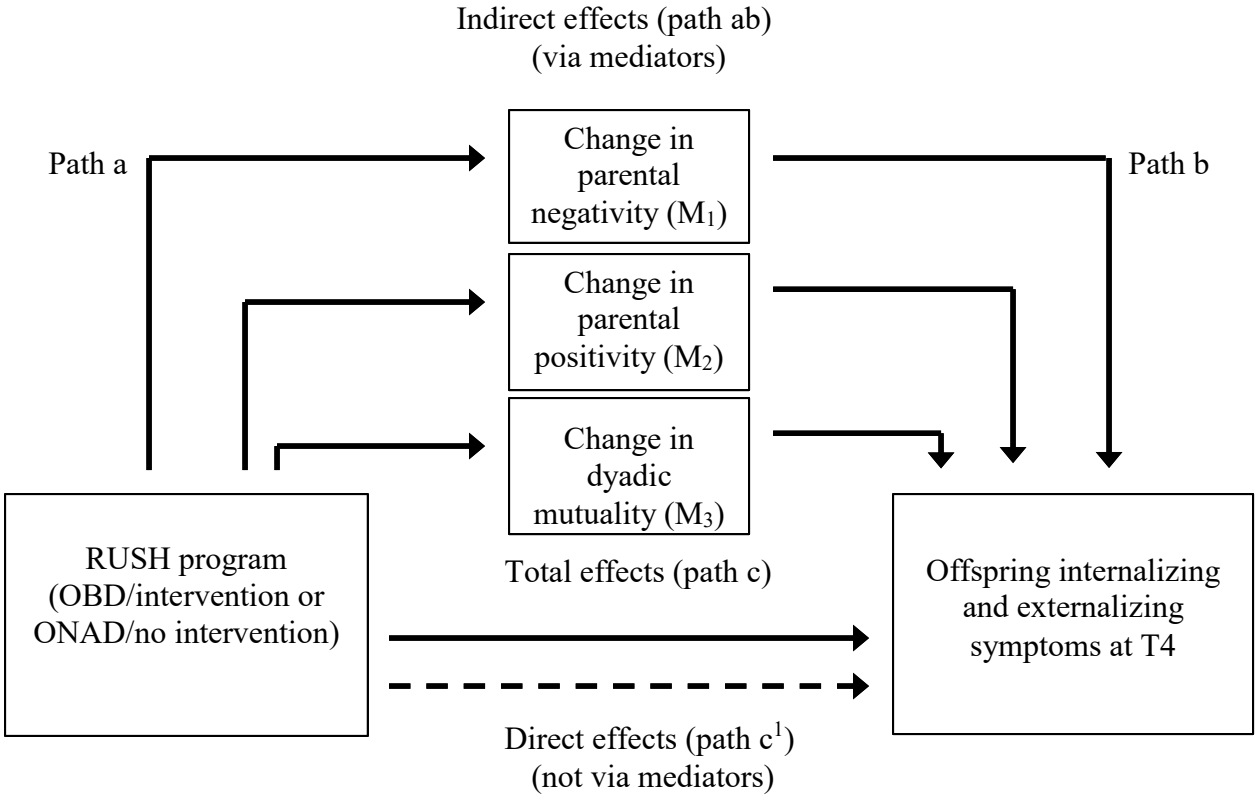


*Figure 3.* Multiple mediation model. Parallel mediators include pre-to-post-intervention change in parental negativity, parental positivity, and dyadic mutuality scores, as calculated by subtracting T2 scores from those obtained at T1. The independent variable is whether or not a family participated in the RUSH program, which should be considered synonymous with offspring risk status (having a parent with BD or not). Offspring internalizing (anxiety, depression, somatization) and externalizing (hyperactivity, aggression, conduct problems) symptoms at T4 (6-month follow-up) is the outcome. OBD = offspring of parents with bipolar disorder; ONAD = offspring of parents with no affective disorder; M = mediator.

## Chapter 4: General discussion

The OBD constitute a population at high risk for experiencing a host of psychiatric problems throughout the lifespan (e.g., Rasic et al., 2013), possibly as a result of a complex interplay between genetically-transmitted traits and exposure to adverse environments (Brietzke et al., 2012). Concurrently, theoretical and practical interest in preventing maladaptive outcomes in the OBD prior to the development of more serious mood disorders has been increasing. To this end, the results from the two studies that comprise the present dissertation add to a growing body of literature investigating environmental risk factors in the OBD and highlighting the key role played by the caregiving environment in determining mental health outcomes in this population. Namely, in study 1, which utilized a longitudinal design, parents with BD reported significant impairments in parenting practices relative to parents without a history of affective illness, providing less support (i.e., emotional warmth), structure (i.e., organization and consistency), and control (i.e., disciplinary strategies) to their offspring during middle childhood. Importantly, low levels of structure and control in middle childhood mediated the associations between having a parent with or without BD and elevated parent- and teacher-reported internalizing and externalizing symptoms in offspring in middle childhood and approximately 12 years later. To our knowledge, study 1 is the first prospective study, spanning a decade, to find evidence of mediation via the caregiving environment, suggesting that parenting practices used during middle childhood may represent a causal mechanism in the relation between growing up with a parent having BD and offspring psychopathology. These data further imply that, even for highly heritable disorders like BD, manipulations of the caregiving environment via an intervention might be of benefit to the offspring. The results of study 2 provide preliminary evidence of this prediction.

More specifically, study 2 followed-up the results from study 1 by showing that participation in a 12-week prevention program entitled Reducing Unwanted Stress in the Home (RUSH) led to improved parental positivity (i.e., positive affect and control like laughter and praise), negativity (i.e., negative affect and control like anger and criticism), and dyadic mutuality (i.e., coherent, synchronous mutually warm and cooperative interaction) during interactions between parents with BD and their offspring. In turn, and at least partly consistent with the findings from study 1, pre-to-post improvements in parental negativity and positivity mediated the relation between having participated in the RUSH program and lower rates of parent- and

teacher-reported internalizing symptoms among the OBD six months later. Although interpretations are limited by the use of a quasi-experimental design, study 2 constitutes the first research project to provide evidence of efficacy for a selective prevention intervention expressly designed to benefit the OBD in childhood and prior to the emergence of clinically significant symptoms of an affective disorder. These data are consistent with research using a modified version of Family-Focused Therapy (FFT-HR), as an indicated prevention of BD among OBD reporting early symptoms of the disorder (Miklowitz et al., 2008; 2013; 2014). Importantly, through a number of randomized controlled trials (RCTs), these studies have shown that 12 weeks of family-based intervention can delay onset or hasten recovery from depression among the OBD up to two years later. FFT-HR targets primarily adolescent samples of OBD who already present with notable signs of a major affective disorder, including meeting diagnostic criteria for pediatric BD. One RCT of FFT-HR to date has targeted OBD as young as age 9 years, although the mean age for this sample was 13 years (Miklowitz et al., 2013). In contrast, the RUSH program was designed to target an earlier point in the clinical course of major affective disorders by intervening in OBD aged 6 to 11 years without significant mood symptoms. Ultimately, both selective and indicated prevention approaches to wellness may represent a comprehensive way of addressing risk associated with having a parent with BD.

As aforementioned, two distinct lines of research currently permeate the literature on the quality of childrearing in families with a parent having BD: studies that focus on describing general aspects of the home environment and those that aim to characterize the nature of dyadic relationships within the family unit. This lack of integration has led to important limitations in elucidating the nature of the associations between childrearing and psychopathology in the OBD, especially relative to the abundance of research synthesizing the literature on family functioning and parent-child bonding in the context of unipolar depression in parents (e.g., see England & Sim, 2009; Gotlib & Goodman, 1999 for reviews). Through this dissertation, an attempt was made to begin to reconcile these two family-based areas of research for the OBD, wherein parenting practices representing three aspects of how families with a parent having BD function as a whole (e.g., amount of organization provided by parents in the home) and interaction quality measured at the level of the parent-child dyad were the topics of interest in the first and second dissertation manuscripts, respectively.

In fact, when comparing the results derived from each manuscript, important patterns of commonality emerge. Namely, the two studies provide key evidence that childrearing factors during middle childhood pertaining to both general parenting practices and intra-familial relationships may represent causal mechanisms through which the OBD become at increased risk for mental health problems from middle childhood into early adulthood. Moreover, across the two dissertation manuscripts, specific aspects of the childrearing environment were found to have a differential impact on the mental health outcomes of the OBD. For example, in study 1, levels of parent-provided structure underlay the relation between BD in a parent and offspring psychopathology during middle childhood, but parental control emerged as the strongest predictor of mental health problems in the OBD during late adolescence and young adulthood. In study 2, a decrease in internalizing symptoms among the OBD, as reported by parents and teachers, were each attributable to post-intervention changes within two separate components of parent-child interaction: parental negativity and positivity, respectively. Thus, both manuscripts provide evidence that the effects of suboptimal childrearing on offspring mental illness may be contextualized, suggesting that distinct components of parenting practices and parent-child interaction may represent orthogonal constructs that contribute uniquely to psychopathology in the OBD and should potentially consist of different targets for intervention.

Conversely, an important area of discrepancy between the two dissertation studies concerned the type of mental health outcome that was significantly predicted by an aspect of the caregiving environment. More specifically, wherein low levels of parent-provided structure and control were associated with the development of both internalizing and externalizing symptoms in the OBD in study 1, improved parent-child interaction quality following participation in the RUSH program was predictive of reduced internalizing, but not externalizing, symptoms six months later in study 2. The latter results are consistent with research showing that FFT-HR is especially beneficial for improving symptoms on the internalizing spectrum of mental illness among the OBD (see Miklowitz & Chung, 2016 for a review) and suggest that emotional, compared to behavioral, problems in the OBD may be more amenable to family-based intervention. It is also possible that certain methodological factors, including sample size (i.e., sample size in study 2 was one fourth that of study 1), offspring age and timing of data collection (i.e., middle childhood v. late adolescence, early adulthood), type of informant (i.e., offspring, parent, teacher), and type of assessment tools used (i.e., clinical interviews v. questionnaires),

may explain differences in findings between the two dissertation manuscripts. Unfortunately, such investigations are beyond the scope of the present dissertation.

Ultimately, the literature on childrearing, prevention, and offspring mental health within the context of BD in a parent remains underdeveloped. This is especially true compared to the wealth of theoretical and intervention research that exists on the topics of parenting with depression and its effects on offspring psychosocial development and mental health (e.g., England & Sim, 2009; Goodman & Gotlib, 2002). Unfortunately, it may not be possible to generalize the literature on the offspring of parents with MDD to the OBD, given important differences between MDD and BD. At a phenotypic level, manic episodes and their associated behaviors, including engagement in risk-taking and maladaptive goal-directed actions, are not part of MDD. As it pertains to genetics, heritability rates for BD are at least twice as large as those reported for MDD (see Craddock & Forty, 2006; Wray & Gottesman, 2012 for comparisons). In a study involving 67 twin pairs, McGuffin and colleagues (2003) found that the genetic vulnerability to mania is correlated with, but mostly distinct from, risk for depression, suggesting that BD and MDD should continue to be viewed as separate diagnostic entities despite some degree of commonality. Relative to MDD, BD has also been correlated with more frequent illness episodes, mood variability, and hospitalizations, and a pattern of lesser anxiety (see Cuellar, Johnson, & Winters, 2005 for a review). As such, it is likely that the OBD are exposed to parental behaviors that are, at least to some extent, qualitatively distinct from the caregiving environment within which the offspring of parents with MDD are raised. Additionally, assortative mating, or the tendency for individuals with comparable psychiatric presentations to become involved romantically more often than predicted by chance, has been found to be strongest for BD relative to MDD (see Mathews & Reus, 2001 for a meta-analysis). This has additional implications with regards the caregiving environment; the OBD being more likely than their high-risk counterparts to grow up with two parents exhibiting serious mood problems. In fact, 31% of the intimate partners of parents with BD described in the first study of this dissertation had at least one episode of MDD in their lifetime (Serravalle, Iacono, Hodgins, & Ellenbogen, 2018).

**Are levels of chaos, disorganization, and instability in the home especially important environmental predictors of mental illness in the OBD?**

One hypothesis that was put forth in the general introduction of this dissertation asked if the presence of chaos, disorganization, and instability in the early caregiving environment might represent a specific and primary mechanism through which the OBD are susceptible to psychopathology later throughout the lifespan.

Past research highlights the presence of chaos, disorganization, and instability within the caregiving environment of the OBD, as evidenced by elevated levels of marital conflict and separation (Lam et al., 2005), parental absenteeism (Pini et al., 2005), use of ineffective disciplinary techniques (Calam et al., 2012), and exposure to stressful life events (Ostiguy et al., 2009). Likewise, studies that have utilized broad measures of family functioning (e.g., Chang et al., 2001; Romero et al., 2005; Ferreira et al., 2013) have described heightened conflict and disorganization within the caregiving environment of the OBD; although, low levels of cohesion (i.e., emotional bonding) have also been shown to distinguish between families with and without a parent having BD. Disorganization, negative communication styles and affectivity, and poor parental bonding and insecure attachment styles (e.g., Erkan et al., 2015; Meyer et al., 2006; Vance et al., 2008) have also been reported during interactions between parents with BD and their offspring.

As it pertains to the specific association between childrearing and psychopathology in the OBD, levels of chaos, disorganization, and instability, relative to cohesion and emotional support, may play a more dominant role. Other than the research presented in this dissertation, only two studies to date have investigated if aspects of the caregiving environment might mediate the relation between having a parent with BD and offspring mental health problems. Schudlich and colleagues (2008) found evidence for a small, but statistically significant indirect pathway from parent BD to offspring's current BD via heightened levels of family conflict. Using measures of family cohesion and dyadic bonding, Lau and colleagues (2018) were unable to find similar evidence for mediation. Nonetheless, these data remain at least partly consistent with the results of the present dissertation. Namely, while all aspects of parenting practices and parent-child interaction investigated in the two dissertation manuscripts were shown to be suboptimal in the OBD, only some predicted mental health problems in this population. Low levels of parent-provided structure and control, relative to support, underlay the relation between having a parent

with BD and offspring internalizing and externalizing difficulties in study 1. In study 2, pre-to post-intervention changes in parental negativity and positivity, but not dyadic mutuality, emerged as primary predictors of internalizing symptoms among the OBD. Thus, across both manuscripts, parental behaviors pertaining to relational warmth and emotional bonding were compromised in families with a parent having BD, but did not significantly mediate the relation between offspring risk status and mental health.

As aforementioned, there is also evidence to suggest that the OBD may constitute a unique high-risk population that, through the inheritance of certain characteristics, are especially susceptible to the adverse effects of chaos, disorganization, and instability within the caregiving environment. For example, when compared to healthy controls, the OBD display elevated rates of neurocognitive deficits that both co-exist with and precede the development of psychiatric symptoms (Balanza-Martinez et al., 2008; DelBello & Geller, 2001; Klimes-Dougan, Ronsaville, Wiggs, & Martinez, 2006). In typically-developing youth, organized and consistent caregiving promotes the emergence of executive functions (Hughes & Ensor, 2009; Schroeder & Kelley, 2009; 2010) that, in turn, has been negatively correlated with internalizing and externalizing problems (e.g., Hugues & Ensor, 2011). Ultimately, this may hold especially adverse implications for the OBD who present with neurocognitive impairments that may primarily interact with exposure to a stressful and chaotic home environment to trigger a range of psychiatric conditions throughout their lifespan. There is comparable evidence to suggest that neurobiological abnormalities, such as weakened frontostriatal connectivity (Singh et al., 2014) and dysregulations in the functioning of the hypothalamic-pituitary-adrenal axis (Ellenbogen et al., 2011), may represent other vulnerability traits to psychopathology in the OBD that are primarily related to disruptions in predictable and consistent caregiving (Ellenbogen & Hodgins, 2009; Singh et al., 2014).

Taken together, it is becoming increasingly evident that the OBD are exposed to a range of suboptimal parenting practices and family interactions throughout their development; although, the presence of disorganization, instability, chaos, and conflict - which add to the daily experience of hassles and stress within the caregiving environment - seems to be especially relevant to understanding the OBD's susceptibility to mental health problems as they mature. This conjecture remains speculative, however, given the limited literature on the role of childrearing on the development of psychopathology among the OBD. Additional large-scale and

longitudinal research that directly compares the effects of different aspects of the caregiving environment on the mental health trajectories of the OBD over time is needed to draw more robust conclusions in this regard.

**Shifting focus from the treatment to the prevention of mental illness in youth**

As previously alluded, there has been growing interest in the last few decades within the field of mental health research and clinical practice to shift from a focus on treatment to preventative approaches that may help avert emotional and behavioral problems in youth *before* they become burdensome. Within the general population, substantial percentages of children and adolescents, approximately 10-20% worldwide, will experience some form of mental disorder during the course of their development (Kieling et al., 2011). Consequently, costs are imposed on society beyond those that are placed onto the individuals themselves; costs associated with healthcare, the criminal justice system, and other social services (see O'Connell, Boat, & Warner, 2009 for a review). At present, efficacy has been established for a number of mental illness prevention programs in both low- and high-risk youth, including for depression, anxiety, aggression, and delinquency (e.g., see Farrington, Gaffney, Losel, & Ttofi, 2017; Werner-Seidler, Perry, Calear, Newby, & Christensen, 2017 for meta-analyses). Conversely, translating empirical knowledge into widespread reductions in the incidence and prevalence of mental disorders has remained a challenge. Strategies for widespread dissemination of evidence-based prevention interventions within the community, and the availability of an infrastructure and financial resources that would support optimal delivery, are lacking (O'Connell et al., 2009).

The RUSH program presented in the second manuscript of this dissertation joins growing clinical and community efforts to promote early detection and prevention of mental health problems throughout the lifespan. Interestingly, participation in the RUSH program yielded favorable mental health outcomes despite not explicitly targeting psychopathology in the OBD or their parents. One possibility is that the program's efficacy lies in its ability to alter developmental processes that stem from the interaction between exposure to suboptimal childrearing environments and the expression of biological markers of risk, such as weaker connectivity between cortical and subcortical brain regions involved in emotion regulation (Ladouceur et al., 2013; Singh et al., 2014) and elevated production of the hormone cortisol in response to stressful environments (Ostiguy et al., 2011). More specifically, by targeting the quality of the caregiving environment through the reduction of conflict and enhancement of

organization, limit setting, and discipline within the home, while simultaneously fostering individual stress coping and resilience, the RUSH program may have halted the development of negative mental health trajectories among the OBD. Transactional processes may also be partly responsible for the observed gains, wherein the promotion of adaptive coping in the OBD may have further contributed to improved parental behaviors during interactions with their offspring. As diathesis-stress (Rosenthal, 1963; Zuckerman, 1999) and transactional (Cicchetti & Toth, 1997) models have been implicated in risk for a range of different psychopathologies, benefits of the RUSH program may extend to other high-risk samples. Adapted versions of the RUSH program for families in which a parent presents with a mental disorder other than BD, but that is similarly characterized by issues in the areas of emotional regulation and impulsivity (e.g., Borderline Personality Disorder), may be of particular interest.

**Strengths and limitations**

The two manuscripts included in the present dissertation make a novel addition to the current literature on the caregiving environment and risk for mental disorders in the OBD. To our knowledge, study 1 represents the first research project to both investigate these associations and test for mediation using a controlled, prospective longitudinal design spanning approximately 12 years. A new selective prevention program that specifically targets environmental risk factors, while promoting individual resilience in the OBD, was introduced in study 2. Other strengths common to both study 1 and 2 are the use of multiple informants (i.e., parents, teachers, and/or offspring) and assessment tools (i.e., questionnaires, clinical interviews, and/or laboratory-based observation), as well as the simultaneous exploration of more than one aspect of the caregiving environment. Moreover, the RUSH program featured in study 2 was developed following prescribed principles of effective prevention intervention, including being based on previous research into the risk and protective factors that impact susceptibility to psychopathology among the OBD.

A number of limitations also need to be considered when interpreting data from the present dissertation. Despite elevated rates of assortative mating in families with a parent having BD (e.g., Mathews & Reus, 2001) and research attesting to the differential impact of mothers' and fathers' parenting strategies on offspring clinical outcomes (McKinney & Renk, 2008; Milevsky, Schlechter, Netter, & Keehn, 2007), neither study evaluated the possible unique effects of growing up with one compared to two mentally ill parents, or independently considered the

perspective of each parent with regards to aspects of the caregiving environment or offspring psychopathology. An attempt was made to explore the effects of parent sex on parent-child interaction quality in study 2. However, as the study sample was small and consisted primarily of mothers, it was impossible to ascertain any clear or consistent pattern of results in this regard. Additional investigation of sex effects via larger samples that present with more comparable rates of mothers and fathers is needed. Likewise, the large heterogeneity of BD suggests that the quality of parenting practices and its effects of offspring symptomology might depend on parents' clinical course and the timing of offspring's exposure to periods of relative wellness versus illness in affected families (e.g., Goodday et al., 2018). Future research should consider these factors as possible moderators of the relation between BD in a parent and mental health problems in the OBD.

Further, while evidence was presented for a significant impact of suboptimal childrearing on internalizing and externalizing problems in the OBD, the influence of other important parent variables, like current symptomatology, degree of social support and life stress, or the presence of trait neuroticism (i.e., a tendency to react with elevated emotionality to stressors), that do not directly represent, but may hold influence over the quality of the caregiving environment were not considered. For example, previous research conducted in the sample from study 1 associated high levels of trait neuroticism in parents with BD with unstable and disorganized caregiving environments in middle childhood that subsequently increased the probability of high-risk sexual behaviors and poor interpersonal functioning in the OBD (Ellenbogen & Hodgins, 2004; Nijjar, Ellenbogen, & Hodgins, 2016; Ostiguy, Ellenbogen, & Hodgins, 2012). The future inclusion of such parent data as interaction terms or control variables would allow for a better understanding of the impact of growing up with and being exposed to the type of caregiving environment that is typically provided by a parent with BD on offspring mental health outcomes.

A particular limitation of study 1 is that parenting practices were only measured during middle childhood. As such, it was impossible to elucidate the type of caregiving environment that might be most pertinent to predicting mental health trajectories in the OBD at different periods of development. Specific limitations also stem from study 2, including the use of an assessment-only control group, which limited conclusions about whether or not the gains made by the OBD would exceed those observed in a different sample of high-risk youth (e.g., offspring of parents with major depressive disorder), an active control group, or OBD not participating in the program

(i.e. wait-list control). The degree to which distinct components of the RUSH program engendered change in parent-child interaction quality or offspring internalizing symptoms could also not be ascertained. Moreover, the sample utilized was small ($n$ = 26 offspring) and, as such, non-significant findings, like with regards to dyadic mutuality or offspring externalizing symptoms, should be interpreted with caution. Lastly, families who participated in the RUSH program were relatively high functioning (i.e., parents from this sample were mainly middle class, employed, and received regular, outpatient follow-up for BD), which may limit generalization to other community samples of families with a parent having BD.

**Future directions**

Prospective, longitudinal studies continue to be needed, as they can provide valuable information about which factors are temporally related to the emergence and to changes in psychological symptoms, as well as refine our current understanding of the aspects of childrearing that are not only suboptimal, but also predictive of mental health problems among the OBD. At present, only a few other prospective longitudinal samples exist to track the development of the OBD as they mature (e.g., Duffy et al., 2014; Hillegers et al., 2005; Radke-Yarrow, 1998; Shaw, Egeland, Endicott, Allen, & Hostetter, 2005); the majority of which have focused on mental health as the outcome of interest. Future research would benefit from lending greater attention to other functional outcomes in the OBD, which can also indicate heightened vulnerability, contribute to the formulation of risk profiles, and inspire the creation of novel prevention strategies for the OBD. In this way, a range of psychosocial and health-related outcomes, including interpersonal and coping skills, personality traits, and engagement in high-risk sexual behaviors, have already been investigated using the sample of adolescent OBD described in study 1 (Nijjar et al., 2014; Ostiguy, 2009). Additional research is required to extend these results and produce practical outcomes, such as in educational and occupational domains.

Likewise, continued pursuit of early "warning" signs that may be indicative of future BD among the OBD, other than the presence of a family history of the disorder, is warranted. Specifically, the identification of factors that render certain subgroups of OBD at higher risk for the development of BD relative to others is important, especially as it pertains to the creation of targeted interventions. To this effect, the search for candidate endophenotypes, or heritable biomarkers, has been accruing interest (Duffy, Jones, Goodday, & Bentall, 2016). For example, the function and structure of certain brain regions that affect attention, memory, motivation, and

reward, such as areas within the prefrontal-limbic system, have been implicated in the pathophysiology of BD (e.g., see Hasler, Drevets, Gould, Gottesman & Manji, 2006 for a review). However, evaluation of candidate endophenotypes in unaffected, first degree relatives of patients with BD is lacking, despite being essential to the recognition of high-risk OBD who are most likely to benefit from prevention efforts. Another comparable line of research has focused on identifying the early behavioral and socio-emotional pathways leading to BD in those at familial risk. Neurodevelopmental, anxiety, and sleep problems in childhood may indicate a trajectory towards more serious affective disorders among the OBD (Duffy et al., 2010; 2012; Meyer et al., 2004). Having a parent with BD who is a lithium non-responder (i.e., current leading pharmacological treatment for BD) has also identified a subgroup of OBD who experience early illness onset and a clinical course characterized by elevated mood variability (Duffy et al., 2002; 2018). Similar to the first dissertation manuscript, which showed a pathway from BD in a parent to offspring mental health symptoms by way of specific parenting practices, growing up with a parent having BD who also fails to provide appropriate levels of structure and control within the home environment may represent a subgroup of "ultra" high-risk OBD. Additional longitudinal research is needed to refine our understanding of the developmental markers that signify heightened risk among the OBD. Relatedly, while the evidence to date supports the involvemIent of a gene-environment interplay in the OBD's susceptibility to mental illness, research that explicitly searches for and identifies such gene-environment interactions is needed.

Further opportunities for gathering the OBD's perspective on variables of empirical interest may also be warranted. In a recent study by Lau and colleagues (2018), offspring reports of mental health were not only shown to differ from that of their parents, but also yielded distinct predictive profiles for offspring internalizing and externalizing problems. There is also evidence to suggest that subjective, rather than objective, experiences hold at least equal, if not greater, influence on individual well-being (e.g., Lloyd, King, & Moore, 2010; Weden, Carpiano, & Robert, 2007). Certainly, this is more difficult to accomplish with younger samples, who may not be able to accurately identify or report on their experiences; although, more and more tools are being developed for suitable use in child populations (e.g., Berkeley Puppet Interview; Ringoot et al., 2013).

Lastly, although study 2 provided preliminary evidence for the benefits of a selective prevention program entitled RUSH, its efficacy over and above a wait-list control condition or alternative forms of intervention, such as those focused on the provision of psychoeducation, remains unknown. Similarly, dismantling research is needed in order to identify the features of the RUSH program that were the active mechanisms of change. For example, it would be interesting to explore if parent coaching sessions, wherein positive parenting and other childrearing-specific advice are imparted to parents, may yield results similar to study 2 while substantially reducing the time and resources needed to run the full intervention. At present, the RUSH program remains in its early stages of development. A next step would be to evaluate the RUSH program's efficacy via a larger RCT and over a longer post-intervention time frame.

**Conclusions**

Overall, the findings reported in this dissertation not only contribute to the literature on the early environmental factors that render the OBD at risk for abnormal development, but also set the stage for future research. Specifically, the present findings suggest that aspects of the caregiving environment during middle childhood may represent a causal mechanism by which the OBD become susceptible to emotional and behavioral problems from childhood into adulthood. Relatedly, these findings also support the view that vulnerability associated with having a parent with BD can be mitigated via an environmental intervention; the results derived from the RUSH program highlighting the benefits of ongoing prevention efforts for the OBD. Ultimately, well-timed and targeted interventions are necessary to limit the intergenerational transmission of psychiatric risk from parents with BD to their offspring, and for the prevention of maladaptive mental health trajectories in this population.

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