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# Vulnerability to Depression in Middle Childhood: The Role of Pubertal Development and Cortisol Reactivity in Risk for Depression

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A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy degree in Psychology

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## Abstract

Depression is one of the most common psychological disorders with rates so high it has been referred to as the “common cold” of mental disorders (Kessler, Berglund, Demler, Jin, Koretz, Merikangas, ... Wang, 2003). Although many studies have investigated associations between risk factors and depression in adolescents and adults, middle-to-late childhood has remained a relatively understudied period of development. This dissertation addresses important gaps in the literature on depression risk in a community sample of children ( $N = 205$ ) over the course of middle-to-late childhood (age 7 to 12 years). In Study 1, I hypothesized that pubertal development strengthens associations between known risks (e.g., parent history of depression, cognitive vulnerability, child temperament, and stressful life events) and future depressive symptoms. Partial support was found for this hypothesis; more advanced pubertal development strengthened associations between maternal depression and stressful life events and children’s depressive symptoms. The purpose of Study 2 was to identify classes of cortisol reactivity to stress and their associations with risk for depression (i.e., parent history of depression, child temperament, genetic variants, parenting quality, and stressful life events), and to determine whether cortisol reactivity mediated associations between risk markers and risk for depressive symptoms. Two reactivity clusters were identified representing normative and impaired reactivity; these were differentially associated with depression risk (i.e., child temperament, genetic variants, parenting quality). I did not find evidence that cortisol mediated associations between early risks and future depressive symptoms. Findings highlight the importance of integrating multiple predictors of depression and cortisol in middle childhood.

*Keywords:* depression, child temperament, puberty, middle and late childhood, cortisol, parent depression, child depression, DRD4, 5-HTTLPR, cognitive vulnerability, stressful life events, parenting quality,

### **Co-Authorship Statement**

Yuliya Kotelnikova, Dr. Patricia L. Jordan, and Dr. Elizabeth P. Hayden are co-authors listed on the manuscript that comprises the first study in this doctoral thesis. Dr. Hayden is the principal investigator on the projects that have provided data for both studies. Dr. Hayden has also provided me with invaluable help in formulating my hypotheses, interpreting results, and conceptualizing my findings to the literature on depression risk in middle-to-late childhood. Yuliya Kotelnikova and Dr. Jordan have been actively involved in data collection for both studies. My own involvement in the two studies is comprised of the following: data collection, video coding, preparation of data for analyses, literature review and conceptualization of hypotheses, data analyses, and interpretation of findings within the context of literature on child depression, pubertal development and cortisol reactivity. Dr. Hayden and Dr. Tony Vernon have also provided support working on numerous drafts of the studies included in this dissertation.

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## Table of Contents

Title Page.....	i
Abstract .....	ii
Co-authorship Statement .....	iii
Acknowledgements .....	v
Table of Contents .....	vi
List of Tables .....	vii
List of Figures .....	x
List of Appendices .....	xv
Chapter 1: General Introduction .....	1
Developmental Psychopathology Approach to Depression and Puberty.....	2
The Importance of Middle Childhood.....	3
Predictors of Depression.....	4
Summary.....	11
References .....	13
Chapter 2: Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression.....	28
Introduction.....	28
Method.....	40
Results.....	52
Discussion.....	53
References.....	56
Tables.....	71

Figures.....	74
Chapter 3: Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood.....	77
Introduction.....	77
Method.....	95
Results.....	107
Discussion.....	110
References.....	122
Tables.....	145
Figures.....	150
Chapter 4: General Discussion.....	152
Strengths and Weaknesses of Study 1 an 2 .....	158
Conclusion.....	160
References.....	162
Appendices .....	167

## List of Tables

Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression Table 1: Correlations between all major study variables.....	71
Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression Table 2: Final model predicting children’s depressive symptoms at follow-up....	72
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Table 1: Correlations among study variables.....	145
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Table 2: Model fit statistics for latent growth class analysis.....	147
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Table 3: Predictors of class membership.....	148

## List of Figures

Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression Figure 1: Timeline showing data collection.....	74
Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression Figure 2: Relationship between maternal depression history and child depressive symptoms at follow-up by child pubertal development.....	75
Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression Figure 3: Relationship between stressful life events and child depressive symptoms at follow-up by child pubertal development.....	76
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Figure 1: Timeline showing data collection.....	149
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Figure 2: Hypothesized mediation model. ....	150
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Figure 3: Latent class models 1-4.....	151
Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood Figure 4: Two class latent growth class model used in all predictor and mediation model analyses. ....	152



## **List of Appendices**

Appendix A: Baseline Ethics Approval Study 1 and 2.....	177
Appendix B: Follow-up Ethics Approval Study 1 and 2.....	178

## General Introduction

Depression is one of the most common psychological disorders, with rates so high that the World Health Organization (WHO) Global Burden of Disease Study ranked depression as the most burdensome disease in the world with respect to total disability (Gotlib & Hammen, 2008; Murray & Lopez, 1996). Referred to as the “common cold” of mental disorders, lifetime prevalence estimates range from 12-24% (Kessler, Berglund, Demler, Jin, Koretz, Merikangas, ... Wang, 2003). Depression is linked to diverse negative outcomes, including work absenteeism (Hees, Koeter, & Schene, 2013), psychosocial difficulties (Cabello, Mellor-Marsá, Sabariego, Bickenbach, & Ayuso-Mateos, 2012), more frequent psychiatric and medical comorbidity (Kessler, Birnbaum, Shahly, Bromet, Hwang, McLaughlin, ... Stein, 2010), as well as greater disability (Satyanarayana, Enns, Cox, & Sareen, 2009). Given these negative physical, psychological, and social consequences, early identification strategies may ultimately help reduce the short- and long-term impact of depression by informing prevention and intervention strategies.

The current overview will begin with a discussion of the importance of a developmental psychopathology framework in the study of depressive disorders. This perspective will be discussed in the context of understanding developmental transitions relevant to depression, particularly pubertal development. This will be followed by a discussion of middle childhood as an important, although relatively neglected, period of development in the study of depression, and evidence for this developmental period as a crucial time frame for identifying youth at greatest risk for depression will be reviewed. Major correlates most consistently found to predict depressive disorders, including parental history of depression, parenting quality, child temperament, cognitive vulnerability, stressful life events, and cortisol reactivity will be

reviewed, and current knowledge of their associations with depression in middle childhood will also be discussed. Finally, this review will present future directions for development of this area in understanding the development of depressive disorders in middle-to-late childhood.

### **The Developmental Psychopathology Approach to Depression**

Guerry and Hastings (2011) noted the importance of a developmental perspective in understanding the nature, etiology and course of depression in youth, for two primary reasons: (1) to articulate and examine transactional models that examine the roles of both biological and environmental influences, and (2) to develop theories that capture the processes by which pathways to mood disorders develop. Similarly, Cicchetti and Toth (1999) stated the importance of integrating developmental processes at multiple levels of biological, psychological and social complexity of individuals over the life course. This approach is inherently multidisciplinary in that it integrates knowledge of developmental, clinical, neurobiological and other areas within a developmental framework to understand the complex nature of depressive disorders. One important feature of depression discussed by Cicchetti and Toth (1999) is its etiological heterogeneity; that is, depression has multiple causes and emerges via different developmental pathways. Approaches to studying depression that focus on individual risk factors do not account for the fact that there are multiple risks that lead to depressive disorder onset and maintenance of symptoms across time.

Another feature of a developmental psychopathology approach to the study of depression is the use of longitudinal methods. Until fairly recently, most work on depression risk has used cross-sectional designs. Although these studies may provide insight into relevant risk factors for depressive disorders, they do not allow for the study of developmental processes or change across development (Rutter & Sroufe, 2000). One major developmental transition relevant to

depression is pubertal development (Angold, Costello, & Worthman, 1998). Although there have been cross-sectional studies examining pubertal development and its associations with depression (Kaltiala-Heino, Kosunen, & Rimpela, 2003; Marcotte, Fortin, Potvin, & Papillon, 2002; Petersen, Sarigiani, & Kennedy, 1991), there has been limited research on whether pubertal development moderates associations between risk markers (e.g., parent history of depression, temperament) of future depressive symptoms. As some of the most prominent predictors of depression in adolescence and adulthood often show weak or no associations with depression in childhood (Hankin & Abramson, 2001), it is possible that pubertal development represents an important stage during which the effects of various risks for depression observed in adolescent and adult samples emerge.

### **The Importance of Middle Childhood**

Many developmentally informed studies of depression have focused on infants of depressed mothers (Field, 1995; Goodman & Brand, 2009; Tronick & Reck, 2009) and adolescent-onset depression (Fergusson, Horwood, Ridder, Beautrais, 2005; Petersen, Compas, Brooks-Gunn, Stemmler, Ey & Grant, 1993; Rudolph, 2008). Unfortunately, one of the most understudied developmental stages, but perhaps also one of the most important for understanding depression onset, is middle childhood. Middle childhood is a time of important emotional, physical, cognitive, and social changes (McHale, Crouter, Tucker, 2001), and may be particularly informative with respect to the development of depression compared to earlier childhood, as children this age are more likely to show emerging variability in depressive symptoms relative to early childhood, yet most will not have presented with full criteria for depressive disorders (Cohen, Cohen, Kasen, Velez, Hartmark, Johnson, ...Streuning, 1993; Zahn-Waxler, Klimes-Dougan, & Slattery, 2000). Given the known predictive validity of

depressive symptoms for the development of clinically significant manifestations of disorder (Boland & Keller, 2009), this developmental period in particular offers an opportunity to study vulnerability for future depressive disorders prior to depression onset. Middle-to-late childhood is also worthy of study as it precedes a dramatic rise in depression during adolescence (Birmaher, Ryan, Williamson, Brent, Kaufman, Dahl, ... Nelson, 1996; Petersen et al., 1993; Thapar, Collishaw, Pine & Thapar, 2012), offering researchers an opportunity to identify potential targets for intervention to reduce risk for future disorder.

### **Predictors of Depression**

The study of depression vulnerability in childhood and adolescence is limited by the lack of comprehensive models of future depressive symptoms. There are often several, parallel lines of research focusing on one or two predictors of depression, although it is likely that depression risk factors may have additive or interactive effects (Hammen, Shih, & Brennan, 2004; Kryski, 2014). The following section will provide an overview of the most robust predictors of depression reported in the literature, and discuss the need to integrate these variables into broader models of depressive symptoms across middle-to-late childhood.

**Parent history of depression.** A history of parental depression is one of the most frequently studied predictors of child depressive symptoms (Cummings, Keller, & Davies, 2005; Gotlib & Goodman, 1999). However, despite this large body of research, children's own depression has been inconsistently tied to parent depression history. The majority of research on this topic has focused on maternal depression (Goodman & Gotlib, 1999), although there is a growing body of literature focusing on fathers' depression, which also shows meaningful associations with children's mental health (Flouri, 2010; Kane & Garber, 2004; Ramchandani, Stein, Evans & O'Connor, 2005). Parental history of depression may increase children's risk

through multiple pathways, including genetic transmission of risk (Kendler, Neale, Kessler, Heath, & Eaves, 1993; McGuffin, Katz, Watkins, Rutherford, 1996), exposure to negative parenting (Lovejoy, Graczyk, O'Hare & Neuman, 2000; Paulson, Dauber, & Leiferman, 2006), greater levels of stressful life events (Hammen, 2005), and via the modeling of depressogenic coping strategies or cognitions exhibited by depressed parents (Alloy, Abramson, Tashman, Berrebbi, Hogan, Whitehouse, ...Morocco, 2001; Garber & Flynn, 2001), among other possible mechanisms. The negative effects of parental depression, such as those related to cognitive styles and parenting, may be present and impact children even when parents have recovered from depressive episodes (Abramson, Alloy, Hogan, Whitehouse, Donovan, Rose, ...Raniere, 1999; Lovejoy et al., 2000). Thus, the influence of parental depression is likely not limited to direct exposure to a currently depressed parent.

**Parenting quality.** Research on parenting style and quality has found significant associations between caregiver behavior and child depressive symptoms (McLeod, Weisz, & Wood, 2007; Morris, Silk, Steinberg, Sessa, Avenevoli, & Essex, 2004). Negative parenting styles are also strongly associated with parent depression history, (Carter, Garrity-Rokous, Chazan-Cohen, Little, & Briggs-Gowan, 2001; Lovejoy et al., 2000; Rapee, 1997); however, parent depression and parenting are infrequently included in the same models testing predictors of child depression. As parenting quality and parent depression are associated with one another, further research integrating both in the same model is necessary to clarify their unique effects.

The majority of literature on parenting and children's depressive disorder risk is focused on mother's parenting (Crnic, Gaze, & Hoffman, 2005; Lovejoy et al., 2000). However, more recent studies examining paternal care have reported similar effects (Wilson & Durbin, 2010), with harsh and withdrawn parenting predicting greater child psychopathology and behavioral

problems (DeKlyen, Speltz, & Greenberg, 1998; Morris et al., 2002; Wood, Repetti, & Roesch, 2004). Milevsky, Schlechter, Netter and Keehn (2007) also report positive parenting styles exhibited by fathers predict greater psychological adjustment in adolescence. Parenting behaviour has also been found to predict child and adolescent peer social and romantic relationships (Brown, Mounts, Bamborn, & Steinberg, 2008; Conger, Cui, Bryant, & Elder, 2000), suggesting that parenting may have both direct effects in relation to child depression as well as indirect associations through its influence on children's future social relationships.

**Cognitive vulnerability.** Negative cognitive styles predict depression in adults (Abramson, Metalsky, & Alloy, 1989), and have also been implicated in risk for depression in children and adolescents (Abela & Hankin, 2008). These cognitive styles are characterized by a sense of hopelessness, negative cognitive distortions, cognitive errors and negative attributions for life events (Abela & Hankin, 2008). There is evidence supporting theories of cognitive vulnerability to depression (CVD) in children, although the effects are generally weaker than those reported in adults (Abela & Hankin, 2008). This may be because depressive cognitions do not emerge until later childhood or early adolescence, when formal operational thinking is developed (Cole, Ciesla, Dallaire, Jacquez, Pineda, LaGrange...Felton 2008). However, inconsistencies in the literature may also be due to methodological issues related to how cognitive vulnerability is typically assessed in samples of children. For example, questionnaire-based assessments of cognitive vulnerability typically used in samples of children may be less effective than laboratory assessments (Garber, Gallerani, & Frankel, 2008). Laboratory assessments such as self-referential encoding tasks (SRET; Kuiper & Rogers, 1979) may be better equipped to assess negative cognitions in younger children as they do not demand the

meta-cognitive skills some argue are needed to complete questionnaire-based measures of cognitive vulnerability in children (Jacobs, Reinecke, Gollan, & Kane, 2008).

Cognitive vulnerability is frequently studied within diathesis-stress models of depression (Abela & Sullivan, 2003; Hankin, Abramson & Siler, 2001; Lewinsohn, Joiner, Rohde, 2001). In these models, CVD is conceptualized as a diathesis which may predict future depressive symptoms when accompanied by the presence of stress (Metalsky, Halberstadt, & Abramson, 1987; Monroe & Simons, 1991). In relation to middle childhood, the onset of puberty is a potential source of stress that may interact with negative cognitive styles to predispose to depression. However, pubertal development in relation to cognitive risk has typically been examined in samples of adolescents rather than middle childhood despite the fact that pubertal development begins on average between the age 9.5 and 12 years (Downing & Bellis, 2009). Children in middle-to-late childhood may find the onset of puberty more difficult in terms of the associated physical and emotional changes (Mendle, Turkheimer, & Emery, 2010) compared to children developing later when the majority of their peers will be experiencing the same changes; therefore, pubertal onset may be particularly relevant to depression at earlier developmental periods such as middle childhood (Hamilton, Stange, Kleinman, Hamlat, Abramson, & Alloy, 2013). Future studies testing associations at this earlier time period are necessary to determine if pubertal status may strengthen associations between children's cognitive style and future depression.

**Child temperament.** Positive emotionality (PE; Compas, Connor-Smith, & Jaser, 2004; Watson, Clark, Carey, 1988), negative emotionality (NE; Kotov, Gamez, Schmidt, & Watson, 2010; Watson, Clark, Carey, 1988), and behavioral inhibition (BI; Williams, Degnan, Perez-Edgar, Henderson, Rubin, Pine, ...Fox, 2009) are key temperament traits implicated in



depression risk. PE reflects an individual's tendency to experience pleasure, and to feel enthusiastic, active and alert (Lonigan, Phillips, & Hooe, 2003). Low PE is associated with depressive symptoms in children, adolescents, and adults (Clark & Watson, 1991; Dougherty, Klein, Durbin, Hayden, & Olino, 2010; Lonigan et al., 2003). High PE may also buffer the effects of potential mediators of depression such as cortisol reactivity to stress (Mackrell, Kotelnikova, Sheikh, Jordan, Singh, & Hayden, 2014) and genetic risk (Hayden, Klein, Sheikh, Olino, Dougherty, Dyson, ...Singh, 2010). In contrast, NE reflects negative emotions such as sadness, anger and distress (Lonigan et al., 2003). High NE is associated with depression in both children and adults (Joiner, Catanzaro, & Laurent, 1996; Kotov et al., 2010; Lonigan et al., 2003), and in a meta-analysis of temperament traits and depression risk, NE was the most robust temperament predictor of depression (Kotov et al., 2010). BI is characterized by low approach and fear and anxiety proneness. The literature on BI has been inconsistent with respect to direct associations between this trait and depression risk (Gladstone & Parker, 2006); however, greater levels of BI has been found in children of depressed parents (Rosenbaum, Biederman, Hirshfeld-Becker, Kagan, Snidman, Friedman, ...Faraone, 2000) and is related to other risks for depression such as negative parenting (Fox, Henderson, Marshall, Nichols, & Ghera, 2005) and cortisol reactivity (Mackrell et al., 2014). Thus, temperament traits may operate as both direct and indirect predictors of future depression as well as affect intermediate pathways to future depression.

**Stressful life events.** Stressful life events are consistently implicated in risk for depression in children, adolescents, and adults (Grant, Compas, Thurm, McMahon, Gipson, & Westerholm, 2006; Hammen 2005). In the infant stress literature, exposure to maternal stress predicts greater child physiological reactivity which has been implicated in depression (Davies &

Sandman, 2010; Essex, Klein, Cho, & Kalin, 2002). In school-age children, exposure to both family and peer stressors is associated with greater depressive symptoms (Ge, Conger, Lorenz, & Simons, 1994; Rudolph & Hammen, 1999). Stressful life events predict the onset of depressive symptoms in previously asymptomatic adolescents (Aseltine, Gore, & Colton, 1994). Stressful life events increase over middle childhood and throughout adolescence in frequency (Arnett, 1999; Compas & Wagner, 1991). This rise in stressful life events may partially be due to the increase in interpersonal stressors experienced due to increased time spent with peers (Garber et al., 2008); interpersonal stress is associated with depressive symptoms in adults (Hammen, 2003), which indicates that this increase in interpersonal stress may be particularly relevant to the increased rates of depression noted in adolescence. How information about stressful life events is gathered and the choice of informant may be important in middle-to-late childhood, as children in this developmental period may experience the strongest impacts of both parent- and peer-related stressors (Rende & Plomin, 1991). In earlier childhood when children are spending the majority of time at home and in adolescence when children experience more freedom to avoid family-level stress, the effects of one domain may be more relevant to risk (Chan, Doan, & Tompson, 2014; Compas, Howell, Phares, Williams & Ledoux, 1989; Conley & Rudolph, 2009). Pre-adolescent children may experience most strongly the effects of both home and peer stressors making them even more prone to depressive symptoms if both are present at this period of development.

**Cortisol reactivity.** Psychophysiological reactivity to stress is also associated with depressive symptoms, most strongly in adults (Burke, Davis, Otte, & Mohr, 2005) but in children and adolescents as well (Essex et al., 2002; Hankin, Badanes, Abela, & Watamura, 2010). The majority of this work has focused on the hypothalamic-pituitary-adrenal (HPA) axis, one of the

major biological stress response systems in humans (Guerry & Hastings, 2011). Cortisol, the hormonal end-product of the HPA axis, has been associated with depression, although the pattern of findings has been somewhat mixed. Both hyper- (Pariante & Lightman, 2008; Rao, Hammen, Ortiz, Chen, & Poland, 2008; Stetler, & Gregory, 2011) and hypo-reactivity (Badanes, Watanura, & Hankin, 2011) following laboratory stressors has been associated with depressive symptoms. However, the majority of these studies have been cross-sectional, leaving it unclear which pattern of reactivity may predict risk for future symptoms, or if they both represent risk for different symptom profiles (e.g., hedonic vs. anhedonic) of depression (Luby, Mrakostky, Hefflinger, Brown, & Spitznagel, 2004).

Guerry and Hastings (2011) called for the mapping of potential changes in HPA axis functioning among individuals at the transition to adolescence. They note that the timing and nature of dramatic rises in stressors at this developmental period coincides with increases in depressive symptoms, and that HPA axis function may play a mechanistic role in depression risk. However, it is unclear whether pre-existing HPA axis dysregulation makes some children and adolescents vulnerable to depression or if dysregulation of the HPA axis is a consequence of depressive symptoms of disorders. Further research in middle-to-late childhood measuring HPA axis before pubertal development, prior to the onset of depressive disorders, may address this gap in knowledge.

**Puberty and Depression.** Rates of depression increase dramatically over the course of adolescence (Nolen-Hoeksema, & Girgus, 1994; Petersen et al., 1993). This increase in depressive symptoms coincides with the onset of pubertal development (Ge et al., 2001). Although there have been many studies of puberty and depression risk (Angold & Costello, 2006; Angold & Worthman, 1993; Conley, Rudolph & Brant, 2012; Hayward, 2003), there is a

surprising scarcity of research testing broader models of depression risk markers and how they relate to depressive symptoms in the context of pubertal development.

Research on pubertal development as a moderator of risk markers for depression has focused on puberty in relation to stressful life events. In particular, research has focused on peer stress with studies finding more advanced pubertal development and higher levels of peer stress to predict future depressive symptoms (Conley et al., 2012). Given this literature, pubertal development may serve as a context in which the effects of other depression risks (i.e., parent history of depression, child temperament) are intensified. This may account for the pattern of generally weaker or nonexistent associations between risk markers (e.g., parent history of depression, temperament) implicated in adolescent and adult depression prior to adolescence. Studies integrating information about children's pubertal development in more comprehensive models of depression risk will address the question of whether puberty moderates risk markers found to reliably predict depression in older samples of adolescents and adults.

### **Summary**

There is a clear need to incorporate multiple risk factors into study designs to better test individual and additive risks as well as interactions between predictors, particularly associations across important developmental transitions such as puberty. Additionally, further research is needed to examine possible mechanisms of risk, such as testing models of cortisol as a potential mediator of future depressive symptoms. Third, longitudinal research designs over critical developmental periods, such as middle-to-late childhood, are necessary in order to better understand factors predicting future depressive symptoms. The following studies will seek to address these issues in the literature. In Study 1, I will test multiple predictors for depressive symptoms in middle-to-late childhood and examine the potential moderating effect of pubertal

development. In Study 2, I will examine different trajectories of cortisol reactivity and predictors of cortisol, seeking to address mixed findings with respect to profiles of reactivity related to depression. In Study 2 I will also examine whether cortisol reactivity may mediate future depressive symptoms. Finally, implications of both studies and how they may inform what is currently known about depression symptoms in middle-to-late childhood will be discussed.

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## **Chapter 2: Vulnerability to Depression in Middle Childhood: The role of pubertal development in risk for depression**

Depressive disorders are among the most burdensome diseases in the world in terms of physical, emotional, and financial costs associated (Cabello, Mellor-Marsá, Sabariego, Bickenbach, & Ayuso-Mateos, 2012; Gotlib & Hammen, 2008; Hees, Koeter, & Schene, 2013). Although depression is rare in childhood (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), in middle childhood, children show increased variability in depressive symptoms (Cole, Tram, Martin, Hoffman, Ruiz, Jacques, & Maschman, 2002). Given the predictive validity of early symptoms for later disorder (Birmaher, Ryan, Williamson, Brent, Kaufman, Dahl, ...Nelson, 1996), variation in early symptoms provides an opportunity for researchers to identify factors that predict early symptoms and thus potentially future disorder (Cicchetti & Toth, 1998; Lewinsohn, Rohde, & Seeley, 1998). Such work is better equipped to identify true vulnerabilities rather than the consequences or concomitants of depression, and can therefore potentially inform early interventions and preventions.

Research on vulnerability to depression has traditionally used narrowly defined etiological theories, and relatively few studies have used multi-method, multi-informant, longitudinal approaches. Given that depression in many cases represents a lifelong, chronic condition (Hölzel, Härter, Reese, & Kriston, 2011), a developmental psychopathology perspective that focuses on early markers of depression and factors affecting the course of this disorder is needed. Such a perspective can be particularly useful in order to identify factors that predict which children become depressed as well as to identify potential protective factors that prevent children who are otherwise at risk from developing these disorders (Cicchetti & Toth, 1998; Goodman & Gotlib, 1999). In addition, while there is more robust evidence identifying

reliable predictors of depression in adults and adolescents (Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000; Pine, Cohen, Gurley, Brook, & Ma, 1998), the literature linking these variables and child depression is less consistent (Klein, Dougherty, & Olin, 2005). Further research is needed to clarify inconsistent findings with respect to predictors of depression in childhood, and factors that may moderate which factors predict depression across time and across important developmental transitions.

One of the most robust findings with respect to depression is that rates of the disorder increase during the transition from later childhood to early adolescence, coinciding with the onset of puberty (Ellis, 2004). This period of development is also associated with increased social, physical and psychological stressors in children's lives (Hamilton, Stange, Kleinman, Hamlat, Abramson, & Alloy, 2014). Identifying factors that exacerbate the negative effects of these increasing emotional and social demands on children's mental health may help identify areas for targeted early interventions and limit children who may go on to develop depression. It is also of interest whether risk factors more consistently associated with depression risk in older samples may become more relevant to depression risk starting at this period of development.

I will begin by discussing puberty as a context through which common predictors of depression may emerge as significant predictors of child depression. This will be followed by a review of the literature on some of the most robust predictors that have been identified with respect to depression risk. In particular, well-established risk markers that have been identified in the adolescent and adult literature, such as parent history of depression (Goodman & Gotlib, 1999; Kane & Garber, 2004; Klein, Lewinsohn, Rohde, Seeley, & Durbin, 2002), negative emotionality (NE; Clark, 2005; Klein, Dyson, Kujawa, & Kotov, 2012), life stress (Hammen, 2005), and cognitive vulnerability (Abela & Hankin, 2008) will be discussed. I propose that

pubertal development may serve as an important developmental transition in which these known markers become increasingly tied to children's depression risk. Specifically, although no studies of which I am aware have tested this possibility, it is possible that pubertal status moderates associations between markers of risk and children's depressive symptoms.

### **Puberty as a Moderator of Risk for Depression**

Pubertal maturation is a biological process involving hormonally driven changes in body stature, composition, and sexual characteristics (Ellis, 2004). Research on depression in adolescence has found that differences in pubertal development are more important than child age in predicting emerging sex differences observed in rates of adolescent depression (Conley, Rudolph, & Bryant, 2012; Hayward, Gotlib, Schraedley, & Litt, 1999). Conley and colleagues (2012) outlined several ways in which pubertal development may confer risk for depression. Pubertal changes may confer negative psychological (e.g., poor body image) and social (e.g., peer exclusion) risks which contribute to depression. Physically, puberty consists of bodily changes that mark physical transitions to adulthood at a time when children may be emotionally and socially unprepared for these changes. Puberty also involves hormonal changes associated with depression (Angold, Costello, Erkanli, & Worthman, 1999; Galvao, Silva, Zimmermann, Souza, Martins, & Pereira, 2014; Mezulis, Salk, Hyde, Priess-Groben, & Simonson, 2014).

Pubertal development can be conceptualized in terms of differences in children's pubertal status and children's pubertal timing (Conley et al., 2012). Pubertal status is defined as one's stage of physical maturation. It has been consistently found that more mature pubertal status is associated with higher rates of depressive disorders as well as higher levels of depressive symptoms and moods (Negriff & Susman, 2011). Pubertal timing (pubertal status relative to age) has also been identified as having links to adjustment (Angold, Costello, & Worthman, 1998).

Earlier-developing children and adolescents may encounter difficulties due to being unprepared for these changes, feeling different from their peers, and lacking social support from peers experiencing similar changes (Hamilton et al., 2014). Similarly, children who develop much later than their peers have also been found to be at risk for depressive disorders (Benoit, Lacourse, & Claes, 2013). Individual differences in pubertal status will be the focus of the current study. It is of interest how the emergence of puberty rather than puberty relative to peers, may affect other known risk for future depressive symptoms. If pubertal status moderates other known risks for depression, future studies addressing pubertal status relative to peers across the pubertal transition would also be of further interest with respect to risk for depressive symptoms and future disorder.

Pubertal development coincides with dramatic increases in rates of depression in adolescence (Abela & Hankin, 2008; Petersen, Compas, Brooks-Gunn, Stemmler, Ey, & Grant, 1993). However, whether puberty moderates other known risks for depression in middle-to-late childhood is unclear. Although on average pubertal development begins between the ages of 9.5 and 12 years (Downing & Bellis, 2009), the typical spike in rates of depression associated with the onset of puberty does not occur until age 13 (Angold et al., 1998). In late childhood, several children are likely experiencing the effects of pubertal development, however associations between risks for depression (e.g., parent depression history, temperament, cognitive vulnerability, stress) and depressive symptoms are not consistently found prior to adolescence (Abela & Hankin, 2008; Durbin, Klein, Hayden, Buckley, & Moerk, 2005). Pubertal development, which is associated with emotional, physical and social changes that may be disruptive to children's lives, may make some children particularly vulnerable to the influence of other risks for depression. Studies testing this hypothesis are needed to clarify the nature of



pubertal development as a risk in itself for depression, as well as a context within which other risks and associations with depressive symptoms may be strengthened.

### **Predictors of Depression**

One limitation with respect to the study of depression vulnerability in childhood and adolescence is the use of one or few predictors in models of future depressive symptoms. There are often several, parallel lines of research extending understanding of one or few known predictors of depression (e.g., parent history of depression, stressful life events) although it is likely that these variables have additive or interactive effects (Hammen, Shih, & Brennan, 2004; Kryski, 2014). The following section will discuss some of the most robust predictors of depression noted in the literature as well as the need to integrate these variables into larger models predicting future depressive symptoms across middle-to-late childhood.

**Parent history of depression.** One of the most robust predictors of depressive disorders in adolescents and adults is a parental history of depression (Goodman & Gotlib, 1999; Klein et al., 2002). Maternal history of depression in particular has been consistently found to predict depressive symptoms in adolescent samples (Bureau, Easterbrooks, & Lyons-Ruth, 2009); however, few studies have examined associations between maternal depression and depressive symptoms in middle childhood and late childhood.

Goodman and Gotlib (1999) proposed mechanisms by which a maternal history of depression may transmit risk to children, including: (1) heritability or genetic factors in depression, (2) innate dysfunctional neuroregulatory mechanisms, (3) exposure to mothers' negative and/or maladaptive cognitions, behaviors, and affect, and (4) exposure to a stressful environment. Although Goodman and Gotlib's paper was specific to maternal depression, it is likely that several of the same mechanisms operate with respect to the risk conferred by paternal

depression. The most straightforward way in which parental depression may affect a child's risk is that it represents a genetic vulnerability to depressive disorders. In this case, a child may inherit some genetic predisposition from his or her mother, father, or potentially both parents. In a study of heritability of major depressive disorders, McGuffin and colleagues (1996) found 46% concordance in monozygotic twins and 20% concordance reported for dizygotic twins and overall estimates of heritability for major depression ranged from 48% to 75% depending on population risks for depression. In addition to inheritance of genetic risk for depression itself, depressed parents may also transmit other heritable vulnerabilities such as personality and cognitive or interpersonal styles (Jang, Livesley, & Vernon, 1996; Kruger, Markon, & Bouchard, 2003; Lau, Rijdsdijk, & Eley, 2006; Vukasović & Bratko, 2015).

More recently, interest in associations between paternal depression and child depression has increased, with findings indicating that paternal depression may also predict child psychopathology (Flouri, 2010; Klein et al., 2005). Highlighting the importance of including paternal depression history in studies of child mental health, Ramchandani and colleagues (2005) found that children whose fathers had depression during the postnatal period were at increased risk for behavioral problems at age three. This study did not include child depressive symptoms as an outcome variable, likely due to the age of the sample of children, so it is unclear if mothers and father's depressive history would differentially predict child depressive symptoms. The authors proposed that paternal depression may have a direct effect on the way in which fathers interact with their children or it may indirectly influence risk through its ties to other predictors, such as increased marital conflict.

It is important to point out that the majority of the literature linking parental history of depression to child symptoms has focused on young children (infancy to age six) or adolescents.

Associations between parental depression history and child depression risk in middle childhood have been less consistent, and less often tested (Birmaher et al., 1996; Luoma, Tamminen, Kaukoken, Laippala, Puura, Salmelin, & Almqvist, 2001). One potential explanation for inconsistencies in the strengths of effects reported in the literature in middle childhood may be that the effect of parental depression, which is more consistently associated with depression risk in adolescents and adults than children (Birmaher et al., 1996; Hammen, Brennan, & Keenan-Miller, 2008), is moderated by pubertal development. Studies of middle childhood often include children ranging from ages 7 to 12, some of whom may already be in the early stages of pubertal development (Angold et al., 1998). It may be that the effects between parental depression and child depressive symptoms become strengthened during this developmental transition, which could partially account for why the findings are less consistent beginning at this period of time given that children in this age group may be more heterogeneous in terms of their physical and psychological development compared to adolescent samples.

**Cognitive vulnerability.** Cognitive theories of depression propose that negative cognitive styles, involving negative self-views and negative views of the world, are a vulnerability factor for depression (Jacobs, Reinecke, Gollan, & Kane, 2008). Two of the most cited models of cognitive vulnerability to depression are Beck's cognitive theory (Beck, 1983), and Abramson, Metalsky and Alloy's (1989) hopelessness theory of depression. Beck's cognitive model (Beck, 1987) defined cognitive vulnerability as characterized by negative self-schemas revolving around feelings of inadequacy, failure, and worthlessness. These schemas are reflected in dysfunctional attitudes and self-worth contingencies. Beck's theory proposes that when people with high cognitive vulnerability encounter negative life events, their negative self-schemas are activated, leading these individuals to develop negative feelings about themselves,

the world, and the future, in turn leading to depressive symptoms. Negative cognitive styles are therefore thought to influence the development of depression by how they lead the individual to interpret and process negative events encountered in their lives (Jacobs et al., 2008).

Similarly, Abramson, Metalsky and Alloy's (1989) hopelessness theory of depression proposed that some individuals have a predisposing tendency to attribute negative events to global, internal, and stable causes, and positive events to specific, external, and unstable causes. This predisposition becomes "depressogenic" in the context of stressful life events, leading to hopelessness and depression. In addition to the literature on attributional styles as a marker of cognitive vulnerability to depression, self-esteem and self-concept have also been linked to the etiology of depression, with low self-esteem and negative self-concept implicated as vulnerability factors conferring risk to depression (Hankin, Mermelstein, & Roesch, 2007; Schmidt & Joiner, 2004; Taylor & Ingram, 1999) in the context of stress (Hankin, Abramson & Siler, 2001).

A large literature has tested the claims of cognitive models of vulnerability to depression, largely finding support for these models in adults (Abela & Hankin, 2008; Gibb & Coles, 2005; Taylor & Ingram, 1999). Although some studies of adolescents have found support for a diathesis-stress model of cognitive vulnerability to depression (Hankin et al., 2001), others have reported main effects of CVD or stress in predicting depression, but no interaction of the two (Hagen, 2009). Cole et al. (2008) found evidence suggesting that the interaction between attributional styles and stress did not predict depressive symptoms until later in adolescence; the hypothesized interaction was not significant in younger children. However, in a review of cognitive vulnerability in children and adolescents, Abela and Hankin (2008) noted that the evidence for these models was generally supportive, with more consistent positive findings

between cognitive vulnerability and depressive symptoms in later childhood and adolescence. However, Ingram and colleagues (2006) noted that the amount of data collected testing these models in childhood, although generally supportive in later childhood, still lags behind those which have been reported in adult samples and that more research is needed.

Despite the general level of support for these models, several questions remain unanswered about the nature of CVD and risk for depressive disorders in childhood. One question related to these findings is whether pubertal development has any effect on associations between CVD and child depressive symptoms. The onset of puberty may be viewed as a stressful event as it is associated with a variety of changes in childhood, both physical and social that may cause distress for some children (Graber, & Brooks-Gunn, 1996). It may be that this period of time in particular moderates associations between cognitive risk and depression such that the more advanced or earlier developing a child is, the stronger the associations will be observed with CVD and depression.

**Negative emotionality.** Temperament is defined as early emerging, stable patterns of behavioral and emotional reactivity with neurobiological underpinnings (Degnan & Fox, 2007; Rothbart & Bates, 1998). While temperament has for the most part been used to refer to individual differences in childhood, there is evidence that several core traits exhibit stability across the lifespan (Caspi, 2000; Caspi, Harrington, Milne, Amell, Theodore, & Moffitt, 2003; John, Caspi, Robins, Moffitt, & Stouthamer-Loeber, 1994; Rothbart & Bates, 1998). Negative emotionality (NE) is a trait evident in all major models of personality and temperament, and refers to proneness to negative emotions including anger, irritability, fear or sadness (Rothbart, Ahadi, & Hershey, 1994).

Several studies have reported associations between NE and future depressive disorders (Joiner & Lonigan, 2000; Lonigan, Phillips, & Hooe, 2003; Verstraeten, Vasey, Raes, & Bijttebier, 2009). In a meta-analysis of literature on temperament and depression, Kotov, Gamez, Schmidt and Watson (2010) reported that both major depressive disorder and dysthymic disorder were associated with high NE (Cohen's  $d = 1.33$ ; Cohen's  $d = 1.93$ , respectively) in adults. This association between NE and depression was stronger than links between depression and other traits examined (e.g., positive emotionality, conscientiousness, and agreeableness). Although this meta-analysis provides strong evidence for the importance of NE and depression risk in adults, it did not include studies of children or adolescents.

However, given that direct associations between temperament traits and depression risk have not been consistently found in studies of children (Durbin, Klein, Hayden, Buckley, & Moerk, 2005), further study is needed to clarify the role of NE in relation to depression risk in childhood. In a community sample of 100 three-year-olds, Durbin and colleagues (2005) found maternal history of depressive disorders was not associated with child NE. As parent depressive history is often used as an index of child depressive disorder risk, it is surprising given the strong effects frequently reported in adult literature that this association was not significant. In a later study using a larger sample of preschoolers, Olino, Klein, Dyson, Rose and Durbin (2010) also failed to find significant main effects of NE and PE predicting depressive symptoms. Thus, there have been mixed associations between NE and depression risk in children; however, it may be that the associations identified between NE and child depressive disorder risk are moderated by other variables such that associations may be strengthened by factors such as other temperament traits, stressful life events, parent depression or pubertal development (Kotelnikova, Mackrell, Jordan, & Hayden, 2014; Mezulis, Hyde, & Abramson, 2006; Verstraeten et al., 2009).

In a review of associations between temperament and internalizing risk, Klein, Dyson, Kujawa, & Kotov (2012) state the critical need for prospective, longitudinal studies. Also of relevance to the current study, future research is needed examining the role of temperament as a function of development. Klein and colleagues also suggest future research testing temperament-environment transactions that may influence predispositions and trajectories for future depressive disorders.

**Stressful life events.** Negative life events are another robust predictor of depression risk in adults (Hammen, 2005; Kessler, 1997). Higher frequency of significant stressors has been associated prior to the onset of major depressive episodes (Hammen, 2005), with the majority of research examining associations between episodic stressors (discrete stress events) and depression risk. However, it is important to note that the majority of people who experience stressful life events do not become depressed. In many cases, stressful life events predict depression in the context of several other interacting or additive risk factors rather than direct stress-depression associations (Compas, Connor-Smith, & Jaser, 2004; Hammen et al., 2004).

The type of stressor as well as the informant reporting on stress have also been found to have variable associations with depression risk (Bogdan & Pizzagalli, 2006). For example, when studying negative life events and associations with depression in children, the type of stressor that predicts risk may be different than those of most relevance to adult depression. Rende and Plomin (1991) asserted the importance of using multiple informants of stressful life events in childhood; collecting information from parents and children on life events may be critical in middle childhood for several reasons. For example, parents may provide better information on stressors involving family finances, parental health, and marital satisfaction (Ge et al., 1994), than their children can at this age. In this case, parent reports may be a critical source regarding

important family-level stressors known to influence child outcomes which children may be influenced by but not be able to report on themselves. However, middle childhood is also a time when peer stressors, on which children may be the more accurate informants, play an increasingly important role in children's lives (Rudolph & Hammen, 1999).

Some researchers have proposed interaction models of puberty and peer relationships (Compas, Hinden, & Gerhardt, 1995; Garber, 2003). In these models, peer stress is thought to exacerbate the negative effects associated with puberty, such that the associations between puberty and depression are stronger when children experience greater levels of peer stress. Although there is a general trend for associations between interpersonal stressors and puberty being stronger for girls, there is also some evidence that this association is true for boys as well (Rudolph, 2008). The main difference observed with respect to boys' and girls' pubertal development and interactions with life stress appears to be in terms of what level of pubertal development (i.e., early versus late developing) represents risk (Benoit et al., 2013). Therefore, it seems as though possible moderators, such as puberty, may be important when studying associations between life stress and depressive symptoms, especially in middle-to-late childhood when children are beginning puberty.

### **Summary.**

The purpose of the current study is to identify associations between multiple risk factors known to be implicated in adolescent and adult depressive symptoms in a sample of children over middle-to-late childhood, and to test whether links between risks and depressive symptoms are moderated by pubertal development. While many studies have examined single or two predictors of risk, few have integrated multiple predictors in risk in a longitudinal sample over this important developmental period. It is important to look at multiple predictors in single



models for the purpose of identifying relative strength of associations between these risk factors and depressive symptoms, as well as to determine if interactions may exist across these risks and depressive symptoms. It is also important to note that variables predicting risk for depression, such as parent history of depression, stressful life events, negative temperament and cognitive vulnerability, are likely interrelated. Including multiple predictors in one model allows testing for unique contributions of each potential risk for future depressive symptoms. Interactions between these risks factors and pubertal status will be examined in order to identify whether the negative effects of these variables (e.g., parent depression, negative temperament, child CVD) may be amplified depending on child pubertal development. As this developmental transition is associated with a variety of physical and psychosocial changes for children, this may represent a time in which children are particularly sensitive to risk. As the literature for the various predictors discussed has been relatively inconsistent in children as compared to adolescent and adult literature, it is hypothesized that the risk factors and their associations with depression risk will be stronger in later stages of puberty as compared to those who have not yet begun or are in early stages of pubertal development.

## **Method**

### **Baseline Sample Characteristics**

The current data were drawn from a longitudinal study of children's depression vulnerability. At baseline, a community sample of 205 seven-year-old children (boys = 96; 47%) and their parents were recruited from London, Ontario and the surrounding areas. Children with a diagnosis of any psychological or developmental disorder were not eligible to participate. The mean age of children at baseline was 88.44 months ( $SD = 3.58$ ; range = 84-96 months), and the mean age of parents was 37.48 years ( $SD = 8.96$ ) for mothers and 40.43 years ( $SD = 11.50$ ) for

fathers. The Peabody Picture Vocabulary Test, Fourth Edition (PPVT-IV; Dunn & Dunn, 1997) was administered; children performed within the normal range ( $M = 111.92$ ;  $SD = 12.15$ ). Parents identified their child's race as Caucasian ( $N = 180$ ; 88%), Asian ( $N = 4$ ; 1.95%) or other ( $N = 16$ ; 7.80%); 2.44% ( $N = 5$ ) of the sample was missing ethnicity data. The vast majority of the children at baseline assessment ( $N = 187$ ; 91%) came from two-parent homes. Approximately half of the families participating ( $N = 103$ ; 50%) reported a family income ranging from \$40,000-\$100,000; 26.83% ( $N = 55$ ) of families reported a family income greater than \$100,000, 15.12% ( $N = 31$ ) of families reported a family income of less than \$40,000 and 7.80% ( $N = 16$ ) of the sample was missing family income data. These sample characteristics are comparable to data pertaining to race and income reported in the 2008 census for London, Ontario (Statistics Canada, 2008), the census closest to when baseline data were collected.

The current study includes a subset of data from the larger study, including measures collected at baseline and two follow-ups, hereafter referred to as Time 2 and Time 3 follow-ups; these occurred when children were aged 9 and 12. The data collection timeline and current study measures obtained at each time point can be found in *Figure 1*. As can be seen in *Figure 1*, predictors vary in terms of the dates collected. This was due to a variety of reasons, such as age appropriateness of measures and time constraints for data collection at each time point. Parent depression history, child temperament and child CVD as indexed by the Self-Referent Encoding Task (SRET) were collected at baseline. Child and parent stress and child self-reported pubertal development questionnaires were collected at Time 3. Children completed the Depression Self Rating Scale (DSRS) as a measure of child depressive symptoms at all three waves; Time 3 depressive symptoms are the dependent variable in all models and reports of depressive symptoms at previous visits treated as a covariate.

## **Child Temperament**

Child NE was assessed using a battery of laboratory tasks based on the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith, Reilly, Lemery, Longley, & Prescott, 1995) adapted to be appropriate for older children. Tasks were designed to simulate naturalistic events likely to be experienced by children in their everyday lives (e.g., being allowed to play with a novel toy, interacting briefly with a stranger, or attempting to complete a frustrating puzzle), and were ordered to minimize carry-over effects in that no episodes presumed to evoke a similar affective response occurred consecutively. Children were also provided with a short break between tasks in order to return to a neutral state. Such laboratory measures of temperament have been shown to tap meaningful differences in children's emotionality and behaviour (e.g., Buckley, Klein, Durbin, Hayden, & Moerk, 2002; Durbin, Hayden, Klein, & Olino, 2007; Hayden, Klein, & Durbin, 2005) and to be related to relevant constructs, such as affective tone during parent-child interactions (Kochanska, Coy, Tjebkes, & Husarek, 1998), emotion regulation (e.g., Buss & Goldsmith, 1998), parental history of psychopathology (e.g., Durbin, Klein, Hayden, Buckley, & Moerk, 2005), as well as genetic (Hayden, Dougherty, Maloney, Durbin, Olino, Nurnberger, et al., 2007) and cognitive (e.g., Hayden, Klein, Durbin, & Olino, 2006) markers of risk for internalizing disorders. Temperament indices derived from this battery also show significant homotypic continuity with the same traits assessed using the original Lab-TAB tasks (Durbin et al., 2007) and are meaningfully associated with children's symptoms (Kotelnikova, Olino, Mackrell, Jordan & Hayden, 2013). Tasks were video-recorded for coding and are described below in the order that they were administered.

*Exploring new objects.* The child was left alone to play freely in a room containing several ambiguous or mildly "scary" objects: a cloth tunnel and tent, a remote-controlled spider,

a plastic skull covered with a red cloth, a Halloween mask, and a box containing a plastic beating heart and fake spider webs.

*Racing cars.* The child was given photographs of an exciting/desirable toy (a remote-controlled race car) and of a relatively boring toy (a small plastic doll with unmoving parts) and was told to choose which s/he wanted to play with. Next, the child was told that the requested toy was lost and was given the non-preferred toy to play with.

*Stranger approach.* The child was left alone in the main experimental area to play with a toy golf set. Following a short delay, a friendly male research assistant entered the room. The stranger attempted to engage the child following a scripted set of prompts and gradually approached the child.

*Frustrating puzzle.* The child was left alone to complete a puzzle that the experimenter said was easy but actually contained pieces that would not fit together. After 3 minutes, the experimenter returned and explained that she had made a mistake and had given the child the wrong pieces.

*Practical joke.* The experimenter showed the child how to use a remote-controlled whoopee cushion, and the child was invited to surprise his/her parent with the toy when they sat in a chair in the experimental room.

*Object fear.* The child was shown a pet carrier and told that it contained “something scary.” The child was instructed to look inside and subsequently left alone in the room.

*Toy parade.* The child was given a bell and told that each time they rang it, a research assistant would bring them a new toy, but that they would have to trade in the toy they had for the new toy. Toys were intended to be fun and included Mr. Potato Head, a Fun Hop, a Gearation Toy, a floor piano and guitar, and Legos.

**Coding procedures.** Undergraduate, post-baccalaureate, and graduate student raters blind to other study data coded all laboratory episodes for affect and behavior. As part of the training process, raters coded individual episodes with a trained “master” coder. Ongoing reliability checks were done to maintain minimum inter-rater reliability (minimum ICC = .80) for all episodes. To assess child NE, each instance of facial, bodily, and vocal NE exhibited by children in each episode was rated on a 3-point scale as low, moderate, or high. Instances of moderate and high behaviors were weighted to account for their greater intensity (e.g., N of moderate intensity smiles\*2; N of high intensity vocal sadness\*3). After weighting, the total numbers of low, moderate, and high intensity NE were summed separately within each channel (facial, bodily, vocal) across the seven episodes.

### **Depression Self-Rating Scale (DSRS)**

The DSRS (Birleson, 1981) is a 24-item self-report measure of depression in children, with items tapping affective, cognitive, behavioural, and somatic symptomatology (Asarnow & Carlson, 1985); it demonstrates good psychometric properties (e.g., Asarnow & Carlson, 1985) and convergent validity (e.g., Ivarson, Gillberg, Arvidsson, & Broberg, 2002). Children are asked to rate themselves regarding how often they experience a depressive symptom (i.e., “most of the time,” “sometimes,” or “never”). The DSRS is thought to be more readily understood by younger children than other child self-reports of depressive symptoms (Costello & Angold, 1988).

The DSRS demonstrates good psychometric properties (e.g., Asarnow & Carlson, 1985) and scores are related to symptoms of depression as assessed by other measures (e.g., Asarnow & Carlson, 1985; Birleson, 1981; Ivarson, Gillberg, Arvidsson, & Broberg, 2002; Kashani, Reid, & Rosenberg, 1989). Total scores on the DSRS were used as an indicator of current depressive

symptoms of children. DSRS scores demonstrated good internal consistency (Cronbach's  $\alpha = 0.73$ ). The average score in the current sample was 12.44 ( $SD = 5.32$ ), comparable to that observed in other nonclinical samples (e.g., Asarnow & Carlson, 1985). Boys and girls scored similarly,  $t(200) = 1.35$ , *ns*, which is consistent with prior research indicating that sex differences in rates of depression are not observed until adolescence (e.g., Hankin, Abramson, Moffitt, Silva, McGee, & Angell, 1998; Hankin, Wetter & Cheely, 2008; Nolen-Hoeksema & Girgus, 1994).

### **Measures of CVD**

**Mood induction procedure (MIP).** In order to produce mild negative affect and activate latent cognitive vulnerability (Taylor & Ingram, 1999; Teasdale & Dent, 1987), a mood induction procedure (MIP) was administered prior to the SRET, in which children were shown a sad movie clip. This method has previously been shown to be successful in producing sad affect in children (e.g., Brenner, 2000), and the specific clips and procedures used here have been shown to increase children's facial expressions of negative affect (Hayden et al., 2006), and to lead to decreases in children's self-reported positive mood (Hayden et al., 2006). The majority of children ( $n = 192$ ; 94%) in the current study viewed a clip from the Disney movie "Flash," which depicted the reaction of a boy to the death of his grandmother. It was important that children had not previously seen the mood induction clip. Children, therefore, were asked prior to being shown the clip if they had already seen the movie. In cases where children reported having seen this movie ( $n = 13$ ; 6%), they viewed one of a series of alternative clips taken from the following films: "My Girl," "Gilbert Grape," and "The Cure." Children were offered the clips in the same order and were shown the first clip they reported not having seen before.

**Self-referent encoding task (SRET).** The SRET (Kuiper & Derry, 1982) is a widely used information processing task used to assess memory biases for positive and negative self-

referent information, as well as the extent to which individuals hold positive and negative self-views. In this task, participants are presented with a series of positive and negative adjectives and are asked to indicate whether each adjective is self-descriptive. This task is followed by an unexpected free recall period in which participants are asked to recall as many of the presented adjectives as possible.

Immediately following the MIP, children were presented with 26 words (13 positive and 13 negative) from previous research using this task with young children (Hayden et al., 2006). Words were presented on flash cards and spoken aloud by the experimenter. Following each word, children were asked “Is this like you?” Words were presented in a random order for each participant with two neutral buffer words presented at both the beginning and the end of the list to address primacy and recency effects. This portion of the task was followed by an unexpected incidental recall period in which children were asked to recall as many of the words as possible from the list.

Two-hundred and three children completed the SRET. Missing data consisted of data from one child who refused to complete the task and one child whose parent did not provide consent for this task to be administered. A negative schematic processing score was calculated (the proportion of negative words rated as self-descriptive and recalled relative to all words rated as self-descriptive). Endorsement rates negative words were also used as measures of self-esteem or self-concept. The average number of negative words endorsed as self-referent was 0.98 ( $SD = 1.57$ ). Boys endorsed more negative adjectives ( $M = 1.35$ ,  $SD = 1.86$ ) than girls ( $M = 0.66$ ,  $SD = 1.19$ ;  $t(201) = 3.06$ ,  $p < 0.01$ ). The average negative processing score was 0.01 ( $SD = 0.03$ ). There were no sex differences for either of the processing scores (both  $p$ -values  $> 0.12$ ).

Both the number of negative adjectives endorsed and the negative processing score demonstrated a high degree of positive skewness and kurtosis, due to a high number of scores of zero. Because there was a range of scores for the number of negative adjectives endorsed, a logarithmic transformation (base 10) was performed on SRET scores. This transformation significantly improved both the skew and kurtosis of the distribution. The range of scores for the negative processing score was quite small, with more than half of the scores being zero. The variable was therefore recoded parametrically, with those children with negative processing scores greater than 0 being coded as 1.

### **Parent Psychopathology**

Parents were assessed for lifetime history of psychopathology using the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996), a semi-structured interview used for making DSM-IV Axis I diagnoses (current and past). The non-patient version of the SCID, a version for use in research studies in which participants are not identified as psychiatric patients (First et al., 1996), was administered to parents. Interviews occurred during a home visit assessment and were administered and scored by graduate students in clinical psychology who were blind to other aspects study data. Inter-rater reliability was assessed by having each interviewer video-record a subset of interviews, which were then rescored by one of the other interviewers. Parents who had ever met diagnostic criteria for major depression (MD) or current dysthymia disorder (DD) were of interest for the current study. Agreement between raters was high, with Cohen's Kappa = 1.00,  $p < .001$  for a diagnosis of any depressive disorder.

In situations in which one of the biological parents was unavailable to complete a SCID (i.e., they were deceased, incarcerated, or the participating parent did not know how to contact



them or did not grant permission for them to be contacted), the Family History-Research Diagnostic Criteria (FH-RDC; Andreasen, Endicott, Spitzer, & Winokur, 1977) was used to obtain an assessment of history of psychopathology. The FH-RDC describes specific operational criteria for determining a diagnosis on the basis of information obtained by the family history method. The FH-RDC was completed based on information obtained from the participating parent by the same clinical graduate student administering the SCID

The majority of mothers ( $n = 202$ ; 98.54%) and most fathers ( $n = 183$ ; 89.27%) completed the SCID. Clinical interview data was obtained via the FH-RDC for one additional mother and thirteen additional fathers. Missing interview data consists of parents (2 mothers and 8 fathers) who were available to participate but refused to complete the SCID or have the co-parent complete the FH-RDC on them.

Parents who had ever met diagnostic criteria for major depression (MD) or dysthymia disorder (DD) were of interest to the current study. These variables were individually coded categorically and later combined into a single score reflecting a lifetime history of depressive disorder. Sixty-eight mothers (33%) had a lifetime history of either major depressive disorder or dysthymic disorder; of these. Thirty-four mothers (16%) had a history of depressive disorders during the child's lifetime. Thirty-four fathers (18%) had a lifetime history of depressive disorders. Fifteen fathers (8%) had a history of depressive disorders during the child's lifetime. Of these parents, 8 mothers (4%) and 7 fathers (3%) met criteria for a current depressive disorder.

## **Time 2 Follow-Up**

Children ( $N = 164$ ; 80% of the original sample) participated in a follow-up laboratory visit designed to assess cortisol responses to social stress approximately 2 years after the initial

assessment (mean time between visits = 2.1 years,  $SD = .35$ ). There were no significant differences in PPVT scores, child sex, child depressive symptoms, SES, ethnicity, family composition (i.e., single versus two-parent homes), or child temperament comparing participants who participated in the follow-up to those who did not (all  $ps > .11$ ). In particular, at follow-up, most children who participated ( $N = 158$ ; 88%) continued to be from two-parent homes.

**Depression Self-Rating Scale (DSRS).** DSRS scores demonstrated good internal consistency (Cronbach's  $\alpha = 0.73$ ). The average score in the current sample was 12.44 ( $SD = 5.32$ ), comparable to that observed in other nonclinical samples (e.g., Asarnow & Carlson, 1985). The DSRS was read aloud to children by a research assistant to address potential reading comprehension problems.

**Adolescent life events questionnaire (ALEQ).** A modified version of the ALEQ (Hankin & Abramson, 2001) was administered as a measure of child self-reported life events. The ALEQ is a 57-item self-report measure of a broad range of negative life events typically reported by adolescents including family problems (e.g., “your parents separated”), school problems (e.g., “got in trouble with the teacher or principal”), and social problems (e.g., “you had an argument with a close friend”). For the present study, items deemed inappropriate for younger children were omitted. Each event is rated for frequency in the past 3 months on a 5-point scale ranging from never (0) to always (4). Total scores on the ALEQ were used as an indicator of child stress<sup>1</sup>. ALEQ scores demonstrated good internal consistency (Cronbach's  $\alpha = .93$ ). The average score in the current sample was 14.02 ( $SD = 10.18$ ).

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<sup>1</sup>The ALEQ contains 3 subscales: family, school, and peer stress. All patterns of correlations and regression analyses were similar across subscales. Therefore, to conserve space, the total ALEQ scores were used in all analyses.

**Parent Self-Reported Stressful Life Events.** Primary caregivers completed a modified version of Dohrenwend's PERI, a 92-item self-report measure of a broad range of negative life events including both acute (e.g., a job change) and chronic (e.g., ongoing financial difficulties) stressors occurring over the past 12 months (Dohrenwend, Krasnoff, Askensay, & Dohrenwend, 1978). Acute life stressors (75 items, e.g., job loss) were rated for frequency in the past year, as well as the degree to which events that occurred were upsetting. To create a composite reflecting the number of acute events and their subjective impact, acute life events scores were computed as the product of the presence/absence score for each event by the impact rating of each event, and summed for a total acute stress score. Chronic stressors (17 items, e.g., "the amount of work or pressure at your job") were rated on a 4-point scale ranging from "not a problem" to "a major problem." A total stressful life events score was computed by summing standardized scores on the acute and chronic life events and this total score was used for all analyses as an index of parent-reported stress.

**Pubertal development scale (PDS).** The child self-report version of the Pubertal Development Scale (PDS; Petersen et al., 1988) was used as a measure of child pubertal status. The PDS consists of rating scales of five characteristics: growth spurt in height, body hair, skin change, breast change (girls only), voice change (boys only), facial hair (boys only), and menstruation (girls only). Each characteristic (except menstruation) is rated on a 4-point scale (1 = *no development*, 2 = *development has barely begun*, 3 = *development is definitely underway*, 4 = *development is complete*). Girls are asked to rate whether they have started menstruating using a dichotomous (yes/no) response. Total PDS scores were calculated with higher scores indicating more mature pubertal status. Good psychometric properties and convergent validity has been

reported for the PDS based on self- and physician-rated Tanner stages (Petersen et al., 1988).

Internal consistencies for PDS in this sample were .62 for girls and .45 for boys at Time 3.

### **Time 3 Follow-Up**

Children ( $N = 150$ , 75% of the original sample) participated in a follow-up laboratory visit designed to assess cortisol responses to social stress approximately four years after the initial assessment (mean time between visits = 2.1 years,  $SD = .35$ ). There were no significant differences in PPVT scores, child sex, child depressive symptoms, SES, ethnicity, family composition (i.e., single versus two-parent homes), or child temperament comparing participants who participated in the follow-up to those who did not (all  $ps > .11$ ). In particular, at follow-up, most children who participated ( $N = 158$ ; 88%) continued to be from two-parent homes.

**Depression self-rating scale (DSRS).** DSRS scores at follow-up demonstrated good internal consistency (Cronbach's  $\alpha = 0.78$ ). The average score in the current sample was 12.44 ( $SD = 5.32$ ).

### **Data Analysis Plan**

A series of hierarchical multiple regression analyses were conducted examining the impact of various predictors of child depressive symptoms at Time 3 follow-up. Specifically, models were run testing main effects of parent history of depression, child NE, life stress, child NE, cognitive vulnerability, and child pubertal status. Further, interactions between each variable and child pubertal status were conducted. It was expected that pubertal development may exacerbate the effects of these risk factors and child depressive symptoms, with stronger associations found between the various risk factors and child depressive symptoms in children with more advanced pubertal development.

Following Aiken and West (1991), variables were centered as appropriate, and product

terms for each depression risk variable and children's pubertal development were made. Significant interactions were explored following Hayes and Matthes' guidelines (2009) for testing regions of significance according to the Johnson-Neyman technique (Johnson & Fay, 1950). This procedure uses the asymptotic variances, covariances, and other regression parameters to derive the values of the moderator at which the conditional effect of the focal predictor on the dependent variable transitions from significant ( $p < .05$ ) to nonsignificant.

### **Results**

Correlations between all major study variables are in Table 1. Boys displayed greater NE during the Lab-TAB than girls, and girls had more pubertal features than boys at follow-up. Boys reported greater depressive symptoms than girls at follow-up. Maternal depression was positively correlated with child puberty. Paternal depression was positively correlated with child negative processing scores at baseline and depressive symptoms at follow-up. Pubertal development was positively correlated with child depressive symptoms at follow-up. Surprisingly, stressful life events were not correlated with any study variables.

Hierarchical regression was used to examine predictors of child depressive symptoms at Time 3, controlling for depressive symptoms at baseline. Specifically, the model tested main effects of parent depression, child NE, stressful life events, cognitive vulnerability, and child pubertal status, as well as interactions between each risk marker and pubertal development; nonsignificant interactions were dropped from the final model. Following Aiken and West (1991), variables were centered as appropriate, and product terms for each depression risk variable and children's pubertal development were made. Significant interactions were explored following Hayes and Matthes' guidelines (2009) for testing regions of significance according to the Johnson-Neyman technique (Johnson & Fay, 1950). This procedure uses the asymptotic

variances, covariances, and other regression parameters to derive the values of the moderator at which the conditional effect of the focal predictor on the dependent variable transitions from significant ( $p < .05$ ) to nonsignificant.

The final model can be seen in Table 2. Significant main effects of child sex<sup>2</sup> and paternal depression were found, with boys and paternal depression predicting greater depressive symptoms at follow-up. No significant main effects were found for maternal depression, child NE, SRET negative processing, or stressful life events; however, two significant interaction effects were found involving children's pubertal development, with maternal depression and stressful life events. The effect of maternal depression on children's depressive symptoms was significant for children with greater PDS scores (Figure 1); at low PDS scores, there was no effect of maternal depression history. Similarly, greater stressful life events predicted higher child depressive symptoms at follow-up 3 in children with greater PDS scores (Figure 2); at low PDS scores, there was no effect of stressful life events on children's depressive symptoms.

### **Discussion**

I examined whether pubertal development moderated associations between children's depressive symptoms and parents' depression, stressful life events, children's NE, and negative memory biases. I predicted that greater pubertal development would increase associations between these markers of risk and child depressive symptoms over time. I found partial support for my hypotheses, such that maternal depression and stressful life events were more closely associated with children's symptoms in the context of more advanced child pubertal

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<sup>2</sup> Interactions between child sex and pubertal status were not of interest to the current study, and were not significant predictors of children's depressive symptoms at Time 3 ( $p = .18$ ).

development. The pattern of interactions for maternal depression and stressful life events with child pubertal status was similar: in the presence of more pubertal features, both maternal depression and stressful life events predicted greater depressive symptoms. In contrast, no relationship between maternal depression and stress was found when pubertal features were low. These findings suggest that puberty may confer risk for depression by heightening the negative effects of other vulnerabilities (Conley et al., 2012), and suggests that middle childhood may be an important time to target children with depression risk for preventative efforts.

I did not find main effects of maternal depression, stressful life events, child NE, or negative memory biases on children's depressive symptoms. This is somewhat surprising given the strength of associations reported for these variables typically reported in studies of adolescent and adult depression. However, as previously mentioned, these variables have been less often examined in middle childhood, and they are not frequently tested within broader models predicting depressive symptoms. It is also possible that some of these influences may become more important later in childhood or in early adolescence, or within the context of interactions with other vulnerabilities not measured here. It may also be the case that some of these influences are more important for boys than girls; interactions with sex were not the focus of the current study, and could not be tested in our already large models.

I found a significant main effect for child sex such that boys reported greater depressive symptoms than girls. Although girls typically report greater depressive symptoms in early adolescence, this is consistent with evidence finding greater depressive symptoms in boys in earlier childhood (Angold, Costello, & Worthman, 1998). I also found a significant main effect of paternal depression, predicting greater child depressive symptoms at follow-up. This finding supports the growing literature emphasizing the importance of fathers' depression on child

vulnerability (Mackrell et al., 2014). In low-risk, community samples such as ours, fathers may be particularly important influences as they may be more likely to be directly involved in children's care.

This study had a number of strengths. I used a multi-method, longitudinal design that spanned a developmentally important period. I tested associations between maternal and paternal depression, instead of focusing solely on mothers. I used structured clinical interviews, observational methods of child temperament, and laboratory assessments of child cognitive vulnerability. However, our study also had several weaknesses. Although the sample size was relatively large, the models included many terms; future replications confirming the interactions observed in this study are important. The reliability of the PDS in this sample was low/moderate, although consistent with findings that reliability for this measure tends to be lower when used with younger children (Bond, Clements, Bertalli, Evans-Whipp, McMorris, Patton, ... Catalano, 2006). I did not collect hormonal measures of pubertal development, which would allow us to make more specific claims about which aspects of puberty (i.e., biological versus psychosocial; Angold & Costello, 2006) were important in moderation of risk. Also, I assessed parent- and child-reported stressful life events using questionnaire measures. Future replication using interview-based methods, considered the gold standard for assessing stressful life events, would be beneficial to replicate findings with respect to stressful life events.

In summary, I found evidence that pubertal development heightens associations between key depression risk markers and depressive symptoms in middle childhood. These findings contribute to the relatively small body of research examining broader frameworks for depression risk in middle childhood.



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Table 1

Correlations between all major study variables

	1	2	3	4	5	6	7	8	9
1. Child sex	--								
2. Mother depression history	.01	--							
3. Father depression history	-.03	.14 <sup>†</sup>	--						
4. Child NE	-.25**	-.04	-.02	--					
5. SRET negative processing	-.09	-.07	.16*	.05	--				
6. Stressful life events	-.08	-.09	.01	.13	.13	--			
7. Puberty	.17*	.15*	-.02	-.05	.00	-.11	--		
8. DSRS T1	-.09	.09	.08	.06	.12 <sup>†</sup>	-.04	.01	--	
9. DSRS T3	-.16*	.08	.16*	.11	.02	-.12	.17*	.40**	--
MEAN	--	--	--	.00	.01	.00	2.00	12.93	9.19
SD	--	--	--	3.26	.03	.72	.38	5.48	4.20

<sup>†</sup>  $p < .10$ ; \*  $p < .05$ ; \*\*  $p < .01$ .

Note: for child sex, boys were coded as '0' and girls as '1', for parent depression, no parental depression was coded as "0" and a history of parent depression as "1." NE = Negative Emotionality, SRET= Self-Referent Encoding Task, DSRS = Depression Self-Rating Scale.



Table 2

*Final model predicting children's depressive symptoms at follow-up.*

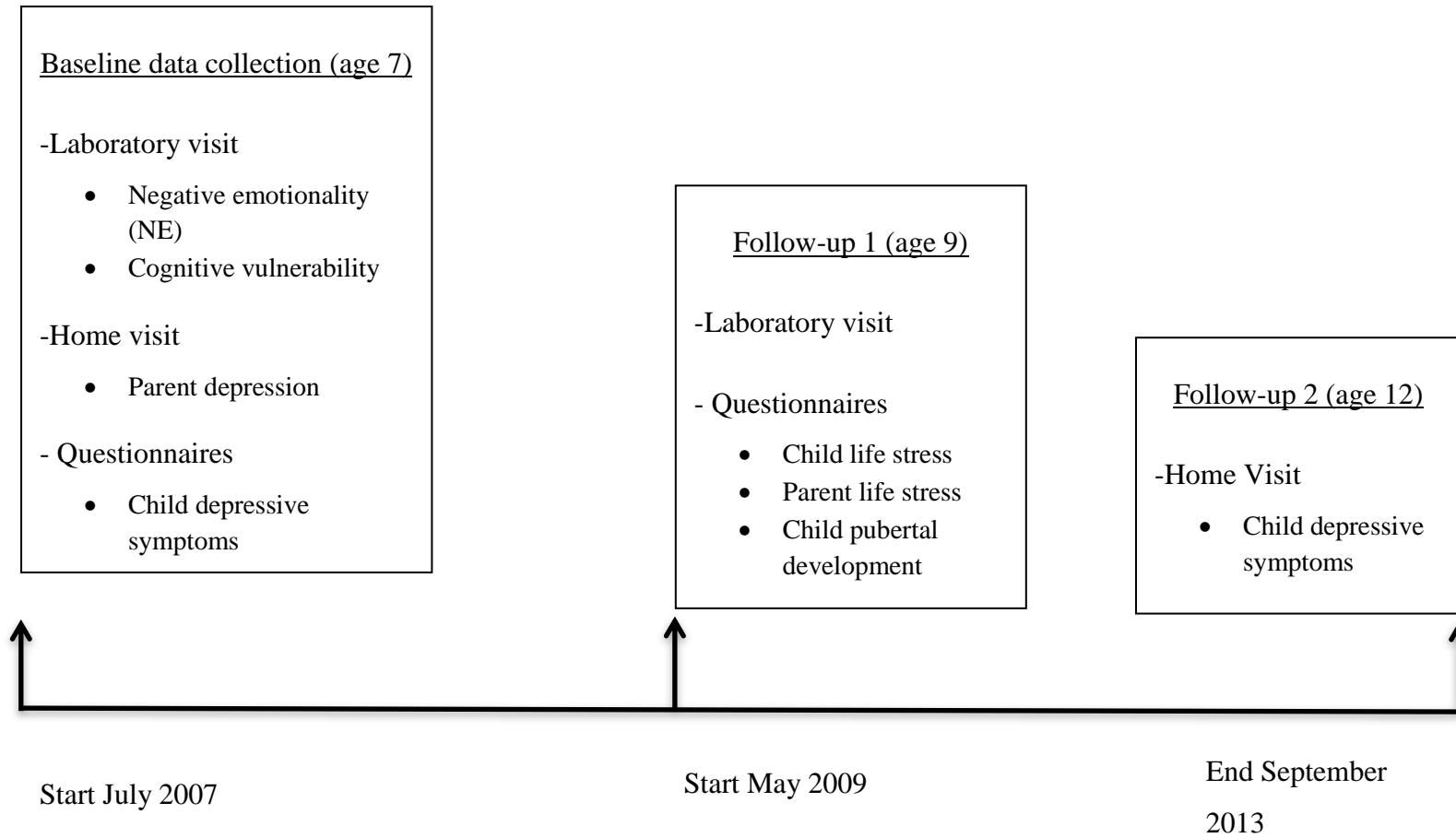
<i>Variable</i>	<i>Standardized coefficient (b)</i>	<i>Unstandardized coefficient (<math>\beta</math>)</i>	<i>Unstandardized SE</i>	<i>pr<sup>2</sup></i>	<i>T</i>
DSRS T1	.23	.18	.06	.06	3.14**
Child sex	-.20	-1.66	.64	.05	-2.60**
Maternal history of depression	-.01	-.17	.68	.00	-.24
Paternal history of depression	.16	1.73	.81	.03	2.14*
Child NE	.05	.06	.10	.00	.50
SRET negative processing	-.05	-6.41	9.67	.01	-.66
Stressful life events	-.09	-.52	.43	.01	-1.20
Puberty	.09	.96	.99	.01	.97
Maternal depression x Puberty	.24	4.44	1.70	.05	2.61**

Stressful life events x Puberty	.15	2.60	1.32	.03	2.00*
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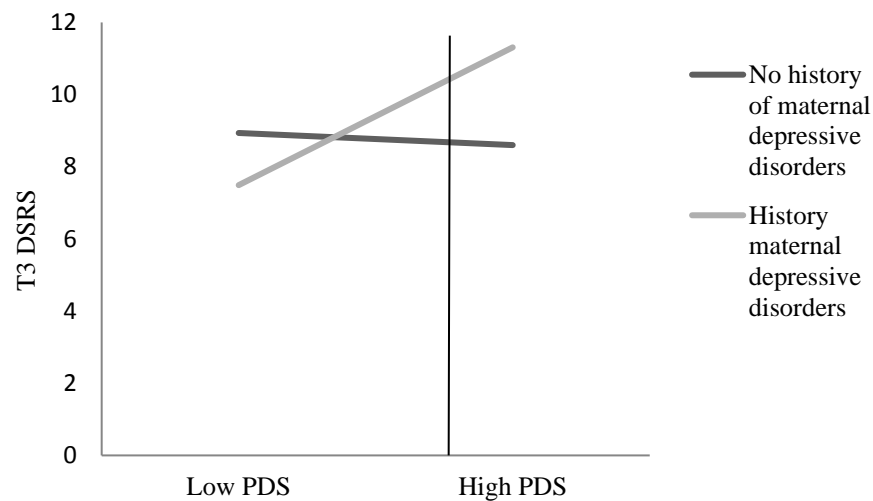
\*\* $p < .01$ , \*  $p < .05$ ;  $N = 155$ ,  $R^2 = .254$ ,

Note: for child sex, boys were coded as '0' and girls as '1'; for parent depression, no parental depression was coded as "0" and a history of parent depression as "1". DSRS = Depression self-rating system, NE = Negative Emotionality, SRET = Self-Referent Encoding Task. Model 1: Adjusted  $R^2 = .155$ ,  $F = 3.83^{**}$ , Model 2: Adjusted  $R^2 = .221$ ,  $F = 5.85^{**}$ .

Figure 1. Timeline showing study data collection.

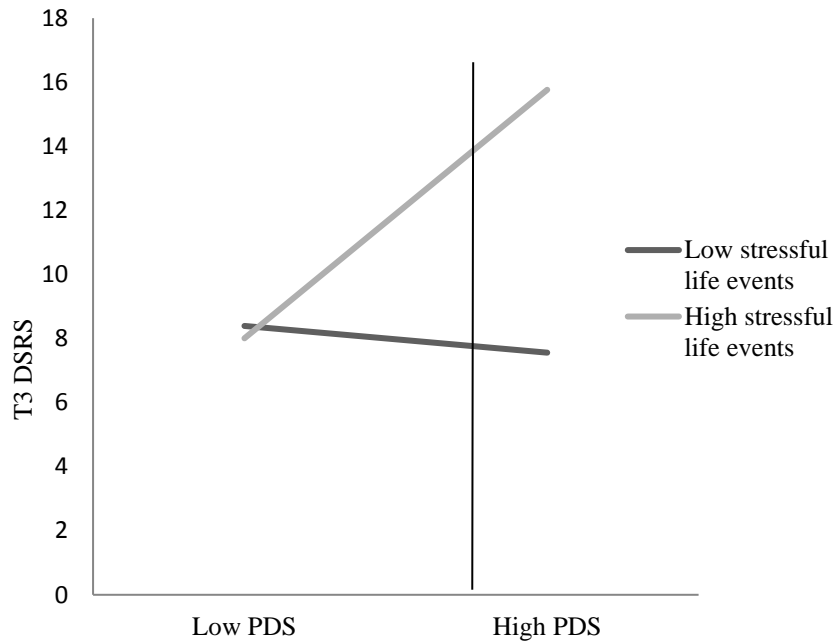


*Figure 2.* Relationship between maternal depression history and child depressive symptoms at follow-up by child pubertal development.



Note: The value  $x = 2.04$ , derived from the Johnson-Neyman technique (Johnson & Fay, 1950), indicates the value of PDS scores above which the effect of maternal history of depression on child depressive symptoms is significant ( $p < .05$ ). Tests of simple slopes between maternal history of depression and child depressive symptoms were significant only for children with a history of maternal depression.

Figure 3. Relationship between stressful life events and child depressive symptoms at follow-up by child pubertal development.



Note: The value  $x = 2.00$ , derived from the Johnson-Neyman technique (Johnson & Fay, 1950), indicates the value of PDS scores above which the effect of stressful life events on child depressive symptoms is significant ( $p < .05$ ). Tests of simple slopes between stressful life events and child depressive symptoms were significant only for children with high stressful live events.

### **Chapter 3: Cortisol Reactivity as a Marker of Depression Risk in Middle Childhood**

The occurrence of a stressful life event is one of the most robust predictors of the onset of depression (Brown, Bifulco, Harris, & Bridge, 1986; Gurrey & Hastings, 2011). However, the mechanisms that account for why stress confers depression vulnerability are unclear, and many individuals who experience stress do not become depressed. This latter observation suggests the importance of identifying individual differences that account for why some react more negatively to the experience of stress than others.

Individual differences in psychophysiological reactivity to stress may be an important explanatory mechanism that marks vulnerability to adversity. One way to index such differences is through activity of the hypothalamic-pituitary-adrenal (HPA) axis, which has been related to depression in many studies (Fernald, Burke, & Gunnar, 2008; Gurrey & Hastings, 2011; Burke, Davis, Otte, & Mohr, 2005; Pariante & Lightman, 2008). The HPA axis is comprised of several structures involved in the body's reaction to stress, including the paraventricular nucleus (PVN) of the hypothalamus, the anterior lobe of the pituitary gland, and the adrenal gland (Smith & Vale, 2006). Cortisol, the end product of the HPA axis, can be indexed noninvasively through salivary assays and is therefore an especially useful tool for studies aiming to characterize differences in activity of the HPA axis system in children (Kryski, Smith, Sheikh, Singh, & Hayden, 2011). This research has the potential to inform our understanding of early depression vulnerability related to maladaptive psychophysiological responses to stress.

Standardized laboratory stress tasks are one of the most commonly used method of eliciting differences in cortisol reactivity (Gunnar, Talge, & Herrera, 2009; Lopez-Duran, Hajal, Olson, Felt, & Vazquez, 2009). The use of such tasks to elicit cortisol, rather than relying on cortisol responses to naturally occurring stress, has value insofar as it allows for the control of

extraneous variables known to influence cortisol reactivity, such as time of day (Dickerson & Kemeny, 2004). Controlled stressors used in the assessment of cortisol reactivity in youth have varied widely, and include public speaking tasks, anger and frustration paradigms, and parent-child conflict, among others (Gunnar et al., 2009; Lopez-Duran, Hajal, Olson, Felt & Vazquez, 2009), with no clear “gold standard” task established as the most relevant means of eliciting cortisol in children. However, in a meta-analysis of studies of adults, Dickerson and Kemeny (2004) identified characteristics of stress tasks that appear key to eliciting a cortisol response in adults; these include unpredictability, uncontrollability, and social-evaluative threat. Additionally, Gunnar and colleagues (2009) reviewed stress paradigms used with youth with the goal of reviewing their efficacy in eliciting cortisol responses to stress. Although not a meta-analysis, their review concluded that public speaking tasks similar to those used with adults were a particularly effective means of eliciting a cortisol response in middle-to-late childhood.

It is important to note the complex associations reported between cortisol responses to laboratory stressors and depression, with some studies implicating cortisol hyperreactivity in depressive symptoms (Pariante & Lightman, 2008; Rao, Hammen, Ortiz, Chen, & Poland, 2008; Stetler, & Miller, 2011) and others implicating cortisol *hyporeactivity* in depression (Badanes, Watamura, & Hankin, 2011). While some of this variability may be due to methodological differences across studies, these seemingly contradictory findings are consistent with the notion that these two reactivity patterns reflect etiological heterogeneity within depressive disorders (Burke, Fernald, Gertler, & Alder, 2005; Harkness, Stewart, & Wynn-Edwards, 2011; Ouellet-Morin, Odgers, Danese, Bowes, Shakoor, Papadopoulos, ...Arseneault, 2011; Suzuki, Belden, Spitznagel, Dietrich, & Luby, 2010). More specifically, these differences may reflect variability in risk factors (e.g., chronic exposure to stressful life events, genetic risk, child temperament,

etc.) that are in turn associated with distinct symptom profiles in depression (Ge, Conger, Lorenz, & Simons, 1994; Meadows, Brown & Elder, 2006; Wickrama, Wickrama, & Lott, 2010). These profiles may similarly be reflected in distinct profiles of cortisol reactivity in children at risk for depressive disorders. Such a notion would be supported by work showing that different patterns of reactivity are meaningfully related to other, well-established risk factors for depression (e.g., temperament, stressful life events). Additionally, given the known predictive validity of early depressive symptoms for later disorder (Pine, Cohen, Cohen, Brook, 1999), it is important to test whether different patterns of reactivity are related to early emerging symptoms. Thus, if cortisol profiles are differentially related to risk markers for depression, they could ultimately be used as indices of risk, which could have implications for early identification and targeted interventions.

Key limitations of the extant work on depression and cortisol reactivity include the reliance on cross-sectional methods, and the fact that most studies have focused on adults. Additional research is needed, particularly from a developmental psychopathology perspective, integrating longitudinal designs that recruit children prior to the onset of depressive disorders (Burke et al., 2005; Herbert, 2013); these are needed to disentangle factors which may predispose children to depressive disorders from those which may be a result of heightened depressive symptoms or disorder. More specifically, in individuals already experiencing significant depressive symptoms, it is less clear which factors contribute to symptoms versus the alternative possibility: that risks increase as a result of experiencing depression (e.g., depressive symptoms predict future stressful life events; Rudolph, Hammen, Burge, Lindberg, & Daley, 2000; Safford, Alloy, Abramson, & Crossfield, 2007).



Accordingly, there has been growing interest in examining children's cortisol reactivity and associations with child depressive symptoms prior to the onset of depressive disorders (Hankin, Badanes, Abela, & Watamura, 2010; Shirtcliff & Essex, 2008), although findings have been less consistent than those reported in adults and adolescents. In particular, there may be age-related changes in youth associated with the relationship between cortisol reactivity and vulnerability. More specifically, cortisol hyperreactivity appears to be a correlate of depressive symptoms and depressive disorders in adolescents (Goodyer, Herbert, Altham, Pearson, Secher, & Shiers, 1996; Hankin et al., 2010), while both blunted- and hyper-reactivity have been associated with pre-adolescent children's depressive symptoms (Hankin et al., 2010; Luby, Heffelfinger, Mrakotsky, Brown, Hessler, & Spitznagel, 2003). These differences may stem from developmental changes that influence associations between HPA axis dysregulation and depression (Hankin, 2012). However, as few studies have examined trajectories within samples using longitudinal designs, this possibility has not been adequately tested. Alternatively, these differences may be due to methodological issues, such as the types of stressors typically used in studies with children versus adults (i.e., fear and frustration paradigms vs. socially evaluative stress tasks). In addition, few studies have examined trajectories of cortisol reactivity in samples of middle childhood to characterize cortisol responses prior to adolescence to determine if they are more in line with those which have been observed in young children or adolescents.

Also, few studies have examined cortisol reactivity to stress in middle-to-late childhood, and whether classes of children can be identified based on such stress responses. This is an important gap in the literature given that depression is often a heterogeneous condition (Chen, Eaton, Gallow, & Nestadt, 2000; Wickrama et al., 2010) and, as mentioned previously, different classes of cortisol reactivity may reflect differences in both risks factors and future symptoms of

those who go on to develop depressive disorders. In one of the few studies of this issue, Ji and colleagues (2016) examined classes of reactivity in a longitudinal study of children ages 8- to 13-years-old. Children completed a modified version of the Trier Social Stress Test for Children (TSST-C) at three time points and authors examined classes of cortisol function at each time point as well as change in class membership over time. A three-class solution was selected for all three time points as best characterizing patterns of reactivity and recovery. In one class of reactivity, children showed an attenuated cortisol response with decreasing cortisol levels over the course of the five time points (i.e., low reactivity and slow recovery), in the second class, children showed a pattern of moderate reactivity and recovery, and children in the third class showed a pattern of heightened reactivity to the TSST-C and slower recovery. The authors found moderate stability in class membership over time; four groups were identified that showed patterns of initial high reactivity, but decreased response to the stressor over time, consistently attenuated cortisol response, moderate levels of cortisol response initially, increasing over time, and consistently high cortisol at all three waves and delayed recovery. However, as this study was focused on characterizing patterns of cortisol response following stress rather than examining predictors of these differences, it is unclear which variables were associated with class membership or change in class membership over time.

A related study by Koss and colleagues (2013) examined classes of cortisol reactivity following an interpersonal stress task in which children were exposed to parental conflict. They identified three classes of reactivity post-stress: falling reactivity, blunted reactivity, and rising reactivity over three time points (baseline, conflict and resolution). The class characterized by an increase in cortisol post-stress and no recovery to baseline levels was associated with a history of child-related conflict, perceived threat, and children's emotional insecurity. Children showing

this profile of reactivity also had the highest rates of concurrent and subsequent internalizing and externalizing problems. This study is of importance as it examined associations between classes of cortisol reactivity following stress and meaningful predictors of stress (e.g., exposure to marital conflict) and child outcomes (e.g., concurrent and future internalizing and externalizing symptoms). However, this study was limited in that only three samples of cortisol were collected following exposure to the stress-task, limiting the ability to examine differences in reactivity to stress, as differences in recovery could not be tested using contemporary statistical analyses (e.g., models of quadratic change could not be tested). Also, the class with the majority of children showed an unexpected pattern of cortisol response, characterized by high baseline levels and decreasing reactivity post-stress. The absence of increase in cortisol post-stress may have been a result of the type of laboratory stressor used. Although the parent conflict task used has high ecological validity, similar types of tasks (e.g., Stroud, Foster, Papandonatos, Handwerker, Granger, Kivlighan, & Niaura, 2009) have also failed to elicit an increase in cortisol post-stress.

Another outstanding issue concerns the extent to which cortisol reactivity plays a mediating role in accounting for links between established vulnerability markers and the emergence of depressive disorders. Cortisol may mediate links between risk factors such as parent history of depression and stressful life events and children's own depressive symptoms (Dockray, Susman, & Dorn, 2009; Tse & Bond, 2004), although few studies have tested this model using longitudinal methods, and none has tested this model in children, a group at low-risk for depression. If interventions can be put in place prior to the age of onset of depressive disorders, the emotional and economic costs of these disorders could potentially be reduced (Beardslee, Wright, Gladstone, & Forbes, 2007).

### **Predictors of Cortisol Reactivity.**

Although there are many factors that have been examined in relation to cortisol reactivity, the current review will focus on the five that have been most consistently implicated in the context of depression risk: stressful life events, parent history of depression, parenting quality, child temperament and genetic variants (Caspi, Sugden, Moffitt, Taylor, Craig, Harrington, ...Poulton, 2003; Durbin, Klein, Hayden, Buckley, & Moerk, 2005; Hammen, Shih, & Brennan, 2004; Klein, Lewinsohn, Rohde, Seeley, & Durbin, 2002; Morris, Silk, Steinberg, Sessa, Avenevoli, & Essex, 2004). With the goal of articulating a model in which early vulnerabilities are mechanistically linked to depressive symptoms via the cortisol response to stress, each section that follows will review evidence for associations between established markers of depression risk and children's depressive symptoms and cortisol reactivity (see *Figure 2*).

**Stressful life events.** Rudolph and colleagues (2000) found evidence that interpersonal stress was the strongest correlate of child depression. Given that social relationships become increasingly important in children's lives in middle-to-late childhood (Conley & Rudolph, 2009; Parker & Asher, 1993), the ability to successfully manage potentially stressful social situations may become more relevant to depressive disorder risk at this time more so than earlier in development. In addition to child-level social stressors implicated in depression risk, family-level stressors are also a strong predictor of child symptoms (Hammen et al., 2004). Parent divorce and high parental conflict have been associated with greater of risk for depression in youth (Gilman, Kawachi, Fitzmaurice, & Buka, 2003) as have family financial stress (Bradley & Corwyn, 2002; Clark-Lempers, Lempers, & Netusil, 1990). While stressful life events have been identified as a strong correlate of depression risk, mechanisms through which these events confer risk are not known. Differences in physiological reactivity to stressful life events may be a possible mechanism that links stress and depression.

With respect to life stress and its effects on cortisol reactivity, multiple studies have reported positive associations between the experience of life stress and cortisol function (Burke et al., 2005; Goodyear, Tamplin, Herbert, & Altham, 2000; Miller, Chen & Zhou, 2007). In 6-, 8-, and 10-year-old children, Lupien and colleagues (2000) found that low socioeconomic status (SES) predicted greater morning cortisol as early as age six. Luijk and colleagues (2010) also found greater cortisol reactivity in infants of mothers experiencing parenting stress. However, other studies have found that stressful life events, particularly severe and chronic stress, are associated with blunted cortisol (Harkness, Stewart, & Wynne-Edwards, 2011). Blunted cortisol reactivity related to stress has typically been found in higher risk samples; children in such samples are frequently exposed to relatively severe stress such as child abuse or maltreatment (Bevans, Cerbone, & Overstreet, 2008). There have been fewer studies examining different clusters of reactivity and stressful life events in low-risk, community samples. Specifically, it is unclear if blunted reactivity profiles in response to stress may reflect cortisol function which may result from prolonged exposure to severe stressful life events typical of higher risk samples, or if this pattern of reactivity in response to stressful life events would be observed in community samples as well.

These studies show that, although there is a growing body of work studying associations between stressful life events, depression, and cortisol reactivity, the literature is currently both mixed regarding the nature of cortisol vulnerability and limited in scope. Specifically, it is unclear whether cortisol hyper- or hypo-reactivity is typical of individuals experiencing stressful life events, and if these profiles are indicative of risk for future depressive symptoms or disorder. Further research examining the role of more moderate stressors and the effects of life stress in lower risk samples is also needed. Research incorporating stressful life events in larger models

testing associations with cortisol and other predictors of depressive symptoms and cortisol reactivity (e.g., parent depression) may also help account for some of the variability in findings that have been reported.

**Parent history of depression.** Familial depression is one of the strongest predictors of an individual's own risk for depression (Klein et al., 2002). There is also growing evidence implicating parental history of depression in children's cortisol reactivity (Laurent, Leve, Neiderhiser, Natsuaki, Shaw, Harold...Reiss, 2013), with maternal history of depression associated with greater cortisol reactivity in both infants (Essex, Klein, Cho, & Kalin, 2002) and adolescents (Ruttle, Klein, Slattery, Kalin Armstrong, & Essex, 2014). In a longitudinal study by Essex and colleagues (2002) which assessed children at 1-, 4-, and 12-months and again at age 4.5 years, maternal depression beginning in infancy was the strongest predictor of children's cortisol reactivity at age 4.5 years. Similarly, Halligan and colleagues (2004) examined associations between salivary cortisol in 13-year-old adolescents, some of whom had been exposed to postnatal maternal depression. Maternal depression predicted higher mean cortisol across 10 days of sampling as well as greater variability in morning cortisol in adolescents. These associations remained after controlling for current maternal and adolescent depressive symptoms, suggesting that early exposure to maternal depression may be important for shaping HPA axis functioning in youth.

The influence of fathers' depression on children's cortisol reactivity has been largely ignored, with the exception of a few recent studies (Laurent, Leve, Neiderhiser, Narsuaki, Shaw, Harold & Reiss, 2013; Mackrell, Sheikh, Kotelnikova, Jordan, Singh, & Hayden, 2014). This is a significant gap in the literature, especially given growing evidence for significant associations between paternal depression history and children's mental health (Ramchandani, Stein, Evans &

O'Connor, 2005). For example, a meta-analysis by Kane and Garber (2004) found significant associations between paternal depression and offspring internalizing psychopathology, and Ramchandani and colleagues (2005) found that fathers' depressive symptoms during children's lives were associated with multiple negative outcomes in a sample of three-year-old children. With respect to paternal depression history and children's cortisol, Laurent and colleagues (2013) found that paternal depressive symptoms had a significant main effect on the daytime cortisol in a study of adopted offspring, and that paternal and maternal depressive symptoms interacted to predict child cortisol, with paternal symptoms heightening the effect of mothers' symptoms on children's cortisol. However, this study relied solely on parental self-reported depressive symptoms covering a limited time frame, and did not examine aspects of children's cortisol stress reactivity. Mackrell and colleagues (2014) found that fathers' depression history predicted greater baseline cortisol and child's cortisol as indexed by area under the curve with respect to ground ( $AUC_g$ ). In contrast, mothers' depressive symptoms did not have direct effects on children's cortisol, but were instead moderated by child positive emotionality (PE) such that children with high PE showed a relatively weak association between maternal depression and children's cortisol. These studies suggest that both mothers' and fathers' depression history predict meaningful differences in children's cortisol reactivity.

These studies provide evidence that both mothers' and fathers' depression history are important predictors of children's cortisol reactivity which may be related to different aspects of child HPA axis function. Despite this, few studies have included both mothers' and fathers' depression risk within the same sample in relation to child cortisol. In low risk, community samples where both parents may be more likely to be present and engaged in children's

caregiving, it may be particularly important to include both parents to best understand associations between parent history of depression and children's cortisol function.

**Parenting quality.** Parenting quality is associated with children's depressive symptoms, both as a direct predictor of depression and also as a moderator of other predictors and potential mediators of depression, such as cortisol (Mezulis, Hyde, & Abramson, 2006; Spangler, Schieche, Ilg, Maier, & Ackerman, 1994). Parenting may serve as both a risk and protective factor, serving to put children at greater risk for developing depression in the context of poor parenting (McLeod, Weisz, & Wood, 2007; Morris et al., 2004) and also serving as a potential buffer in the context of other vulnerabilities (Hostinar, Johnson, & Gunnar, 2015). Studies examining links between parenting and child adjustment have typically focused on parental warmth, support, and control, as well as hostile parenting. Negative parenting styles have been associated with poor adjustment in infancy (Kim, Teti, & Cole, 2012), middle-to-late childhood (Shaffer, Lindhiem, Kolko, & Trentacosta, 2013) and adolescence (Haltigan, Roisman, & Fraley, 2013). However, positive parenting styles have also been studied with respect to indices of child adjustment, with positive parenting found to serve as a protective factor in the context of other known risks for depressive disorders (DeLay, Hafen, Cunha, Weber, & Laursen, 2013). Although middle childhood and early adolescence are marked by a growing focus on peer relationships, positive or negative parenting may serve to shape the success of these relationships and thus may have both direct and indirect effects on risk for developing internalizing disorders (Brown, Mounts, Lamborn, & Steinberg, 2008; Fraley & Davis, 2005).

Similar to studies of parenting quality and depression, studies of parenting and child cortisol have typically focused on younger children. For example, Spangler and colleagues (1994) found associations between maternal sensitivity and infant cortisol, with infants of



insensitive mothers showing the greatest increase in cortisol following parent-infant play. Interestingly, Hostinar, Johnson, and Gunnar (2015) found that parental support appeared to reduce the effect of a social stressor (TSST-C) on offspring cortisol reactivity in children but not adolescents. Hagan and colleagues (2011) found that positive parenting moderated the association between negative life events and children's cortisol in children who had experienced the loss of a parent. The authors found that children who experienced greater positive parenting were less reactive than children who experienced lower positive parenting following a stress task in which parents and children discussed topics that they disagreed about.

Although the literature discussed suggests positive parenting may buffer the effects of stress on cortisol reactivity and negative parenting may predict greater cortisol reactivity, research on parenting and children's cortisol continues to be predominantly focused on infants and young children. Given the differences in cortisol reactivity that have been reported across early-, middle-, and late-childhood and adolescence (Hankin et al., 2010), further research testing associations between parenting and children's cortisol in middle and late childhood is needed to clarify whether we may observe similar associations and similar strength of associations between parenting and cortisol as children age.

**Temperament.** A distinct literature has examined the role of children's individual differences, specifically child temperament, and children's cortisol function. This literature has focused almost exclusively on temperamental behavioural inhibition (BI), the tendency to respond to unfamiliar stimuli with reticence, fear, and wariness (Fox, Henderson, Marshall, Nichols, & Ghera, 2005). The evidence generally supports that BI and related constructs, such as fear, are associated with aspects of heightened cortisol activity and reactivity in early childhood (Hastings & Utendale, 2008). Most studies of fear/BI and cortisol reactivity have focused on

infants or preschool-aged children (Buss, Malmstadt, Schumacher, Dolski, Kalin, Goldsmith, & Davidson, 2003; Fox et al., 2005; Schmidt, Fox, Rubin, Sternberg, Gold, Smith & Schulkin, 1997), with less known about temperament and cortisol in later childhood. An additional concern is that most studies of children's cortisol reactivity and temperament have used tasks that elicit acute fear or startle response (e.g., Schmidt & Fox, 1998). An emerging literature suggests that tasks tapping responses to social evaluation may elicit particularly strong cortisol responses to stress in adults (Dickerson & Kemeny, 2004). More recently, comparable tasks have been shown to be effective in eliciting child cortisol reactivity (Gunnar et al., 2009; Kryski et al., 2011). As middle and late childhood have been associated with greater sensitivity to peer and social evaluation (Conley & Rudolph, 2009) these tasks may be particularly potent in eliciting a stress response.

Another significant limitation of the existing literature concerns the gap in knowledge on the role of temperament traits other than BI/fear in predicting children's cortisol reactivity. In particular, the role of positive emotionality (PE) in shaping HPA axis function is not understood, despite its relevance for both depression vulnerability and stress reactivity (Compas, Connor-Smith, & Jaser, 2010; Durbin et al., 2005; Watson, Clark & Carey, 1988; Wetter & Hankin, 2009). PE refers to the tendency to experience positive moods, to be interested in, and engaged with, the environment, and to seek out social interactions (Hayden, Klein, Durbin, & Olino, 2006). PE has relatively specific associations with mood disorder risk (Clark, 2005) compared to other temperament traits, supporting its relevance to childhood depression risk and potential mechanisms of depression risk, including stress reactivity. Peripheral evidence for a role of PE in HPA axis function includes Fredrickson's (2001) "broaden-and-build theory," which proposes that positive emotions buffer the impact of stress, thereby reducing the experience of negative

emotions following negative life events (Tugade & Fredrickson, 2004). Several studies find that PE influences or moderates the effects of negative emotions and other risks in adults; for example, higher PE predicted a more rapid cardiovascular recovery following negative emotional arousal (Tugade & Fredrickson, 2004). Consistent with this literature, PE was found to moderate associations between maternal depression history predicting children's cortisol reactivity in 9-year-old children (Mackrell et al., 2013). It is of interest whether PE may also moderate other known predictors of child cortisol reactivity as well, such as other biological or environmental effects or if direct associations between low PE and cortisol reactivity, similar to those found in studies of depression, may be identified.

Effortful control (EC) is another temperament trait associated with both internalizing symptoms and child cortisol reactivity. EC is a higher-order regulatory system, and consists of lower-order traits including executive attention (e.g., attentional focus and shifting) and the ability to inhibit dominant responses (e.g., inhibitory control) (Kotelnikova et al., 2014). Associations between EC and related traits and depression have been mixed, with evidence for both high and low EC predicting depressive symptoms (Eisenberg, Valiente, Spinrad, Cumberland, Liew, Reiser...Losova, 2009; Muris, 2006; Murray & Kochanska, 2002). Similarly, associations between EC and cortisol have been mixed with some finding associations between high EC and greater cortisol reactivity while others showing the opposite pattern (Finy, Bresin, Korol, & Verona, 2014; Gunnar, Sebanc, Tout, Donzella, & van Dulmen, 2003; Spinrad, Eisenberg, Granger, Eggum, Sallquist, Haugen, ..Hofer, 2009). These differences may in part be due to differences in how EC is conceptualized, with some studies focusing on EC facets of attentional control while others on inhibitory control (Kotelnikova et al., 2014).

Although these studies support the importance of child temperament in shaping individual differences in cortisol function, it is also important to consider these traits in relation to other risks. As previously stated, this literature has largely progressed independent of research on other known predictors, many of which may share variance. Including temperament constructs in models may provide a more comprehensive understanding of the development of children's cortisol reactivity, as well as providing insights into the known associations between temperament and depression.

**Molecular genetic influences.** An increasing number of studies of genetic influences on cortisol function have emerged in recent years (Gotlib, Joormann, Minor & Hallmayer, 2008; Miller, Wankerl, Stalder, Kirschbaum & Alexander, 2013), with a variant in the promotor region of the serotonin transporter gene (5-HTTLPR) receiving particularly close attention. This 43-base pair insertion/deletion polymorphism is thought to influence the transcription rate of the serotonin transporter gene, with the short (*S*) allele being transcriptionally less efficient than the long (*L*) allele (Pezawas, Meyer-Lindenberg, Drabant, Verchinski, Munoz, Kolachana, ...Weinberger, 2005). Although the literature is mixed and controversial (Zammit & Owen, 2006), several studies suggest that there is increased risk for depressive disorders in individuals who are carriers of at least one *S* allele (Caspi, Sugden, Moffitt, Taylor, Craig, Harrington, ...Poulton, 2003; Karg, Burmeister, Shedden, & Sen, 2011; Sheikh, Hayden, Singh, Dougherty, Olino, Durbin & Klein, 2008). For example, Caspi and colleagues (2003) found that individuals with one or two copies of the *S* allele were found to have greater depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events as compared to individuals homozygous for the *L* allele. In addition to studies focused on direct genetic associations with depressive disorders, there is also a growing literature with similar patterns of

findings between the 5-HTT and markers of depressive disorders, such as cortisol (Gotlib et al., 2008).

In a meta-analysis of associations between 5-HTTLPR and cortisol stress reactivity, Miller and colleagues (2013) found a small but significant association, with homozygous carriers of the *S* allele displaying increased cortisol reactivity compared to individuals with the *S/L* or *L/L* genotypes. This association was not moderated by participant age, sex, or stressor type. In contrast to this finding, Mueller and colleagues (2011) found a main effect for young and older adults homozygous for the *L* allele showing a significantly larger cortisol response to the Trier Social Stress Test (TSST) compared to individuals carrying at least one copy of the *S* allele. This pattern of greater reactivity for the *L* allele carriers was not observed in the children. Additional research is needed testing direct effects of the 5-HTTLPR and cortisol in youth, as well as how this association may be implicated in future depressive symptoms.

Gotlib and colleagues (2008) suggested that HPA axis reactivity may be a mechanism underlying associations between 5-HTTLPR, stress, and depression, based on their findings that girls homozygous for the *S* allele showed a marked increase in cortisol secretion following a laboratory stress task. This was in contrast to girls with at least one copy of the *L* allele, who showed a slight decrease in cortisol reactivity over the course of the stress task. As this study included only girls, it is unclear whether this finding would generalize to boys. These authors also did not test whether cortisol mediated 5-HTTLPR and future depressive symptoms which would be of interest for future studies examining associations between genetic risk and risk for depression.

The dopamine D4 receptor (DRD4) is also associated with child psychopathology risk and cortisol. The DRD4 gene, located on chromosome 11p15, codes for a receptor protein on

neuronal membranes throughout the brain and has been linked to effortful control and related constructs (Smith, Kryski, Sheikh, Singh, & Hayde, 2013). The DRD4 gene is highly polymorphic, with the number of repeats ranging from two to eleven (Ding, Chi, Grady, Morishima, Kidd, Kidd, ...Moyzis, 2002). The DRD4 7-repeat allele has been associated with decreased signal transduction efficiency, decreased RNA stability, and decreased protein folding efficiency (Asghari, Sanyal, Buchwaldt, Paterson, Jovanovic, & Van Tol, 1995; Smith et al., 2013), and is hence thought to mark vulnerability to psychopathology.

Although the literature is mixed, the DRD4 7-repeat allele is associated with child cortisol, particularly attenuated cortisol response (Ambruster, Mueller, Moser, Lesch, Brocke, & Kirschbaum, 2009; Buchmann, Zohsel, Blomeyer, Hohm, Hohmann, Jennen-Steinmetz, ..Laucht, 2014), lower effortful control (Smith et al., 2013), risk for externalizing disorders (Kirley, Lowe, Mullins, McCarron, Daly, Waldman, ...Hawi, 2004), and increased risk for internalizing disorders (Schmidt, Fox, & Hammer, 2007). While there is a growing body of literature supportive of associations with externalizing disorders, relatively few have examined associations between DRD4 genotype and child depressive symptoms, particularly in middle childhood.

With respect to associations between DRD4 and cortisol function, Armbruster and colleagues (2009) examined associations between 5-HTTLPR and DRD4 genotypes and cortisol reactivity following the TSST in young adults. The authors found a significant main effect of DRD4 on cortisol reactivity following the TSST, with carriers of the 7-repeat allele exhibiting lower cortisol responses. No significant main effects were identified for 5-HTTLPR and cortisol; however, an interaction between genotypes emerged, such that 5-HTTLPR *L* homozygotes had a lower cortisol response compared to homozygous *S* or heterozygous *L* allele carriers if they also possessed at least one copy of the DRD4 7-repeate allele. Of note, this study did not examine

associations between genotype, cortisol and future symptoms, so it is unclear whether these differences relate to internalizing disorder risk.

As there have been few studies examining associations between 5-HTTLPR and DRD4 and internalizing symptoms and cortisol in middle childhood, additional research is needed focusing on this developmental period. Future research testing cortisol as a mediator of future depressive symptoms may establish whether cortisol serves as mechanism underlying gene-depression associations.

### **Cortisol as a Mediator of Depression Risk**

The preceding review focused on correlational work linking cortisol and depression risk; however, a more compelling approach with greater implications for early identification, prevention, and treatment would be research showing mechanistic links between cortisol and depression. Although maladaptive patterns of cortisol stress reactivity may mediate early vulnerabilities to depression (e.g., genetic risk, Badanes et al., 2011; Gurrey & Hastings, 2011), few studies have tested such models, although there is a small literature in adults (Muhtz, Zyriax, Klähn, Windler, & Otte, 2009). For example, Muhtz and colleagues (2009) found elevated afternoon and evening cortisol to partially mediate the association between metabolic syndromes and depression in women. Tse and Bond (2004) tested two mediation models comparing alternate theories of how cortisol may be associated with depression. First, the authors found evidence that social support mediated the association between cortisol and depression, although cortisol did not mediate the association between social functioning and depression. Although these findings suggest that associations between cortisol and depression may be mediated by other factors rather than serve as a mediator, there are some important limitations to this study. First, the authors used a cross-sectional design, thus precluding tests of longitudinal associations

between the variables of interest and depressive symptoms. Second, the authors' findings may only be applicable to baseline cortisol. Participants provided one saliva sample as an index of HPA axis reactivity. Given that disparate findings have been reported across studies of resting cortisol, morning cortisol, and cortisol reactivity following a stressor, future studies are needed to determine if this finding can be generalized (Burke et al., 2005). It is unclear if baseline cortisol and cortisol reactivity following a stress task would produce the same findings in mediation models predicting depression risk. There are also no studies of which the author is aware that have tested whether cortisol mediates associations between predictors of depression in children. The current study will address this limitation by testing whether cortisol mediates associations between various vulnerabilities and depression at a later follow-up in a sample of children across middle- to late-childhood (see *Figure 2*).

### **Summary.**

The current study will address the limitations of the extant literature discussed in several respects. First, this study will examine potential clusters of cortisol reactivity following a stress task with the purpose of identifying various reactivity profiles. Next, analyses examining various predictors of cortisol cluster groups including stressful life events, parent depression history, parenting quality, child temperament and genetics will be conducted. Finally, mediation analyses will be conducted to test whether these different reactivity profiles mediate the association between known risks for depressive disorders and children's self-reported depressive symptoms at follow-up.

## **Method**

### **Baseline Sample Characteristics**

The current data were drawn from a longitudinal study of children's depression vulnerability. A community sample of 205 seven-year-old children (boys = 96; 47%) and their parents were



recruited from London, Ontario and the surrounding areas. Children with a diagnosis of any psychological or developmental disorder were not eligible to participate. The mean age of children at baseline was 88.44 months ( $SD = 3.58$ ; range: 84 to 96 months), and the mean age of parents was 37.48 years ( $SD = 8.96$ ) for mothers and 40.43 years ( $SD = 11.50$ ) for fathers. The Peabody Picture Vocabulary Test, Fourth Edition (PPVT-IV; Dunn & Dunn, 1997) was administered; children performed within the normal range ( $M = 111.92$ ;  $SD = 12.15$ ). Parents identified their child's race as Caucasian ( $N = 180$ ; 88%), Asian ( $N = 4$ ; 1.95%) or other ( $N = 16$ ; 7.80%); 2.44% ( $N = 5$ ) of the sample was missing ethnicity data. The vast majority of the children at baseline assessment ( $N = 187$ ; 91%) came from two-parent homes. Approximately half of the families participating ( $N = 103$ ; 50%) reported a family income ranging from \$40,000-\$100,000; 26.83% ( $N = 55$ ) of families reported a family income greater than \$100,000, 15.12% ( $N = 31$ ) of families reported a family income of less than \$40,000 and 7.80% ( $N = 16$ ) of the sample was missing family income data. These sample characteristics are comparable to data pertaining to race and income reported in the 2008 census for London, Ontario (Statistics Canada, 2008), the census closest to when baseline data were collected. The current study includes a subset of data from the larger study, including measures collected at baseline, a second follow-up (children age 9), and a third follow-up (children age 12). The data collection timeline and measures obtained can be found in *Figure 1*.

## **Child Temperament**

Child temperament was assessed using an hour-long battery of laboratory tasks based on the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith, Reilly, Lemery, Longley, & Prescott, 1995) adapted for older children. In support of its validity, temperament indices derived from a similar battery show significant homotypic continuity with the same traits assessed using the original Lab-TAB tasks in younger children (Durbin et al., 2007) and are meaningfully associated with children's symptoms in this sample of children in middle childhood (Kotelnikova, Olino, Mackrell, Jordan, & Hayden, 2013). Tasks were video-recorded for coding, and are described below in the order they occurred along with the traits they were designed to elicit.

Exploring new objects (Fear, PE). The child was left alone to play freely in a room containing several ambiguous or mildly “scary” objects: a cloth tunnel and tent, a remote-controlled spider, a plastic skull covered with a red cloth, a Halloween mask, and a box containing a plastic beating heart and fake spider webs.

Racing cars (Anger, Sadness, PE). The child was given photographs of an exciting/desirable toy (a remote-controlled race car) and of a relatively boring toy (a small plastic doll with unmoving parts) and was told to choose which s/he wanted to play with. Next, the child was told that the requested toy was lost and was given the non-preferred toy to play with.

Stranger approach (Fear). The child was left alone in the main experimental area to play with a toy golf set. Following a short delay, a friendly male research assistant entered the room. The stranger attempted to engage the child following a scripted set of prompts and gradually approached the child.

Frustrating puzzle (Anger, Sadness). The child was left alone to complete a puzzle that the experimenter said was easy but actually contained pieces that would not fit together. After 3 minutes, the experimenter returned and explained that she had made a mistake and had given the child the wrong pieces.

Practical joke (PE). The experimenter showed the child how to use a remote-controlled whoopee cushion, and the child was invited to surprise his/her parent with the toy when they sat in a chair in the experimental room.

Object fear (BI, Fear). The child was shown a pet carrier and told that it contained “something scary.” The child was instructed to look inside and subsequently left alone in the room.

Toy parade (PE). The child was given a bell and told that each time they rang it, a research assistant would bring them a new toy, but that they would have to trade in the toy they had for the new toy. Toys were intended to be fun and included Mr. Potato Head, a Fun Hop, a Gearation Toy, a floor piano and guitar, and Legos.

**Coding procedures.** Undergraduate, post-baccalaureate, and graduate student raters blind to other study data coded all laboratory episodes for affect and behavior. As part of the training process, raters coded individual episodes with a trained “master” coder. Ongoing reliability checks were done to maintain minimum inter-rater reliability (minimum ICC =.80) for all episodes. To assess child PE and fear, each instance of facial, bodily, and vocal PE and fear exhibited by children in each episode was rated on a 3-point scale as low, moderate, or high. Instances of moderate and high behaviors were weighted to account for their greater intensity (e.g., N of moderate intensity smiles\*2; N of high intensity vocal sadness\*3). After weighting, the total numbers of low, moderate, and high intensity behaviors were summed separately within

each channel (facial, bodily, vocal) across the seven episodes. Object Fear episode fear counts were excluded from facial, vocal, and bodily fear scales to eliminate overlap between the BI scale and fear coding. This episode was coded for behavioral inhibition as discussed below. Additionally, a single rating on a three-point scale (low, moderate, and high) was made for each of the following behavioral variables per episode, which were then aggregated across all episodes: activity level/vigor ( $\alpha = .81$ ), sociability ( $\alpha = .87$ ), and impulsivity ( $\alpha = .77$ ). Impulsivity was based on the child's tendency to respond and/or act without reflection. Compliance was based on "rule breaking" behavior and the persistence of noncompliance. Impulsivity ratings from each task were reverse-scored and aggregated with compliance ratings from each task used to obtain an index of inhibitory control aspects of EC ( $\alpha = .78$ ). These internal consistencies are comparable to other laboratory measures of temperament (Dougherty et al., 2010; Durbin et al., 2005; Durbin et al., 2007).

Behavioral coding was applied to the Object Fear task, which was designed to assess BI. This coding system was designed to assess traditional behavioral components of BI, such as approach, withdrawal, and fear responses. More specifically, latencies to approach, touch, and look at laboratory stimuli were coded, as well as withdrawal attempts (attempts to leave the room or withdraw from lab stimuli). Tentativeness in interacting with novel stimuli was rated on a 4-point scale. Ongoing reliability checks were done to maintain minimum interrater reliability (minimum ICC = .80) for all episodes. Since variables comprising the BI composite were measured on different scales, they were transformed into z-scores before creating an aggregate. The internal consistency of the BI scale was high ( $\alpha = .95$ ).

An exploratory factor analysis was conducted, which showed that BI (.37) and fear (facial = .25, vocal = .25, bodily = .84) loaded together on a factor we called fear/BI. PE (facial =

.67, vocal = .77, bodily = .74), sociability (.68), activity level (.63), and impulsivity (.33) loaded together on a factor we called PE. While somewhat lower than those found in factor-analytic studies of parent-reported temperament (possible due to reduced method covariance in observational ratings), these loadings are comparable to others reported in factor analyses of laboratory temperament data (Durbin et al., 2005; Dyson, Olino, Durbin, Goldsmith, Bufferd, Miller, & Klein, 2015; Olino, Klein, Durbin, Hayden, & Buckley, 2005). The observed variables were standardized (z-transformed) and then summed within each factor using weightings from the EFA solution.

### **Depression Self-Rating Scale (DSRS)**

The DSRS (Birlleson, 1981) is a 24-item self-report measure of depression in children, with items tapping affective, cognitive, behavioural, and somatic symptomatology (Asarnow & Carlson, 1985); it demonstrates good psychometric properties (e.g., Asarnow & Carlson, 1985) and convergent validity (e.g., Ivarson, Gillberg, Arvidsson, & Broberg, 2002). Children are asked to rate themselves regarding how often they experience a depressive symptom (i.e., “most of the time,” “sometimes,” or “never”). The DSRS is thought to be more readily understood by younger children than other child self-reports of depressive symptoms (Costello & Angold, 1988).

The DSRS demonstrates good psychometric properties (e.g., Asarnow & Carlson, 1985) and scores are related to symptoms of depression as assessed by other measures (e.g., Asarnow & Carlson, 1985; Birlleson, 1981; Ivarson et al., 2002; Kashani, Reid, & Rosenberg, 1989). Total scores on the DSRS were used as an indicator of current depressive symptoms of children. DSRS scores demonstrated good internal consistency (Cronbach’s  $\alpha = 0.73$ ). The average score in the current sample was 12.44 ( $SD = 5.32$ ), comparable to that observed in other nonclinical samples

(e.g., Asarnow & Carlson, 1985). A cut-off score of 17 has been identified as indicative of clinical depression (Asarnow & Carlson, 1985). Boys and girls scored similarly,  $t(200) = 1.35, p > .05$ , which is consistent with prior research indicating that sex differences in rates of depression are not observed until adolescence (e.g., Hankin, Abramson, Moffitt, Silva, McGee, & Angell, 1998; Hankin, Wetter & Cheely, 2008; Nolen-Hoeksema & Girgus, 1994).

### **Parent Psychopathology**

The Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996) was administered to parents during a home visit by graduate students in clinical psychology. Inter-rater reliability was assessed by having each interviewer video-record a subset of 14 interviews, which were then rescored by one of the other interviewers. Agreement was high, with Cohen's Kappa = 1.00,  $p < .001$ , for a diagnosis of any depressive disorder and Cohen's Kappa = 0.83,  $p < .001$  for a diagnosis of any anxiety disorder. Information on psychiatric history was obtained via informant (the spouse) using the Family History-Research Diagnostic Criteria (FH-RDC; Andreasen, Endicott, Spitzer, & Winokur, 1977) for one additional mother and thirteen additional fathers. Missing clinical data consist of parents (2 mothers and 9 fathers) who declined to provide these data.

Major depression and dysthymic disorder were combined into a single category reflecting any lifetime history of depressive disorder. Sixty-eight mothers (33%) had a lifetime history of either major depressive disorder or dysthymic disorder; of these. Thirty-four mothers (16%) had a history of depressive disorders during the child's lifetime. Thirty-four fathers (18%) had a lifetime history of depressive disorders. Fifteen fathers (8%) had a history of depressive disorders during the child's lifetime. Of these parents, 8 mothers (4%) and 7 fathers (3%) met criteria for a current depressive disorder.

## **Observed Parenting**

Observed ratings of parent behavior were made during a structured laboratory task. The primary caregiver and child were provided with a challenging block puzzle and were instructed to work on it together. The puzzle could be solved in six different ways to look like pictures on cards provided. To increase motivation for puzzle completion, the dyad was instructed to place the pictures of completed puzzles in the upper corner of their desk so that the experimenter could see how many they finished after 5 minutes.

**Coding procedure.** Video recordings of the parent-child interaction task were coded by trained graduate and undergraduate raters using a coding manual that was based on the Teaching Task coding manual (Weinfield, Egeland, & Ogawa, 1998) and the Qualitative Ratings for Parent-Child Interactions scale (Cox & Crnic, 2002). Raters were trained to an intraclass correlation of .80 with a supervising graduate student. Reliability for each task was high, ICC > .80). Parent-child interaction tasks were coded on a total of 9 Likert scales: sensitivity, detachment, supportive presence, intrusiveness, hostility, confidence, quality of instruction, positive affect, and negative affect. To reduce the number of analyses, two aggregate scores were created reflecting positive and negative parenting behaviours.

## **Time 2 Follow-Up**

Children ( $N = 164$ ; 80% of the original sample) participated in a follow-up laboratory visit designed to assess cortisol responses to social stress approximately 2 years after the initial assessment (mean time between visits = 2.1 years,  $SD = .35$ ). There were no significant differences in PPVT scores, child sex, child depressive symptoms, SES, ethnicity, family composition (i.e., single versus two-parent homes), or child temperament comparing participants

who participated in the follow-up to those who did not (all  $ps > .11$ ). In particular, at follow-up, most children who participated ( $N = 158$ ; 88%) continued to be from two-parent homes.

**Trier Social Stress Test for Children (TSST-C).** Children participated in a version of the TSST-C (Buske-Kirschbaum et al., 1997). All visits began between 12:00pm and 3:30pm in the afternoon to minimize diurnal variation in cortisol levels. After 30 minutes of quiet resting activity, a baseline salivary cortisol sample was collected. Next, children were brought to the testing room where they were told that they were being asked to complete a story for two “story judges.” The main experimenter provided the beginning of the story and told children that they would have 3 minutes to prepare a middle section and ending for the story. Next, the two research assistants entered the room, and gave children microphone to speak into, and a video camera was held by one of the research assistants. One of the assistants directed children through the TSST-C, prompting them to begin and continue as necessary for a total of 5 minutes. Next, children completed a subtraction task by counting backwards from the number 758 by the number 7 as fast and as accurately as possible, also for 5 minutes. Following this, children were asked to tell the research assistants about themselves and their personality in response to a series of prompts from the research assistants.

In addition to the baseline sample previously described, saliva samples were obtained at ten minute intervals upon completion of the task (i.e., at 0, 10, 20, and 30 minutes following the end of TSST-C) for a total of four samples post-stressor. To collect saliva, children chewed on a dental roll until it was wet with saliva, which was subsequently expunged from the rolls. All samples were frozen immediately following the laboratory visit, and were later taken to a laboratory at the University of Western Ontario to be assayed in duplicate using an expanded range, high sensitivity, salivary cortisol enzyme immunoassay kit (Salimetrics, PA). Cortisol



distributions were positively skewed, as is typical (Gunnar & Talge, 2008); thus, a log<sub>10</sub> transformation of the raw cortisol values was applied.

**Genetic polymorphisms.** DNA was collected from the same saliva samples used to obtain child cortisol data. DNA was extracted using the Qiagen DNA MicroKit according to manufacturer's protocols. Children were genotyped for the serotonin transporter promoter (5-HTTLPR s/l) and dopamine D4 (DRD4 7-repeat present/absent) using allele-specific TaqMan polymerase chain reaction (Sheikh, Hayden, Kryski, Smith, & Singh, 2010). Genotyping was successful for 156 children. Although research regarding the functionality of the 5-HTTLPR s variant is mixed, the S variant was treated as dominant consistent with the bulk of previous studies (e.g., Heils et al., 1996; Steiger et al., 2009) and to limit the number of variables in analyses. DRD4 genotype was coded 7-repeat present/absent. As genotype frequencies vary amongst different racial groups (Gelernter, Kranzler & Cubells, 1997), all significant genetic associations were reanalyzed excluding non-white participants.

### **Time 3 follow-up**

Children ( $N = 150$ , 75% of the original sample) participated in a follow-up laboratory visit designed to assess cortisol responses to social stress approximately four years after the initial assessment (mean time between visits = 2.1 years,  $SD = .35$ ). There were no significant differences in PPVT scores, child sex, child depressive symptoms, SES, ethnicity, family composition (i.e., single versus two-parent homes), or child temperament comparing participants who participated in the follow-up to those who did not (all  $ps > .11$ ). In particular, at follow-up, most children who participated ( $N = 158$ ; 88%) continued to be from two-parent homes.

**Depression Self-Rating Scale (DSRS).** DSRS scores at follow-up demonstrated good internal consistency (Cronbach's  $\alpha = 0.78$ ). The average score in the current sample was 12.44

( $SD = 5.32$ ).

### **Data Analysis**

Previous studies vary in the index of cortisol used (i.e., CAR,  $AUC_g$ , cortisol trajectories over time indexed using multi-level modeling; Kryski, 2014; Lopez-Duran, Mayer & Abelson, 2014; Lopez-Duran, Hajal, Olson, Felt, & Vazquez, 2009). Therefore, to more broadly map the current study methods to the extant literature, I tested models using both  $AUC_g$  and latent class growth analysis (LCGA) classes as mediators of child depressive symptoms at follow-up. Given that  $AUC_g$  and LCGA index different aspects of the cortisol response (i.e., overall cortisol output vs. groups of reactivity and recovery, respectively), I was interested in whether the method of indexing child cortisol may be differentially related to predictors of child depression and future symptoms. I was interested in testing models with both  $AUC_g$  and LCGA classes within the same sample to determine whether differences reported across these indices of cortisol may be identified which cannot be attributed to differences in age or task used. In particular, there may be different risk factors associated with overall cortisol output as compared to children's reactivity and recovery from stress which may be differentially associated with depression risk. As I have previously tested associations between predictors of interest in the current study (i.e., parental depression history, child temperament) and  $AUC_g$  in a previous study (Mackrell et al., 2014), direct associations between variables of interest and  $AUC_g$  were not examined again in the current study.

**Latent class growth analysis (LCGA).** LCGA is a statistical method used to identify class membership based on observed variables. In the current study, LCGA was used to identify groups of children characterized by distinct patterns of cortisol reactivity to the TSST-C. Latent class analyses were conducted using Mplus software (Muthén & Muthén, 1998-2012). Of

particular interest to the current study was whether classes representing blunted, hyper-reactive, and typical reactivity would be identified. Following this, LCGA results were used for mediation analyses to determine classes of reactivity mediated associations between risk factors (i.e., genetics, parenting, etc.) and child depressive symptoms at follow-up.

**AUC<sub>g</sub>.** Area under the curve with respect to the ground (AUC<sub>g</sub>) (Fekedulegn et al., 2007; Pruessner et al., 2003) was calculated using the five samples taken before and after the TSST-C. For endocrinological data, AUC<sub>g</sub> is a measure of total cortisol output (Fekedulegn et al., 2007). AUC<sub>g</sub> was calculated as follows:

$$AUC_g = \sum_{i=1}^{n-1} \frac{m_{(i+1)} + m_i}{2}$$

with  $m_i$  denoting the individual measurement, and  $n$  the total number of measurements. AUC<sub>g</sub> was used in mediation analyses predicting child depressive symptoms.

**Mediation analyses.** Mediation analyses were planned in order to examine whether associations between various risks for child depression (i.e., parent history of depression, parenting quality, genetics, child temperament, etc.) and child depressive symptoms at follow-up were mediated by child cortisol, controlling for baseline depressive symptoms. To test mediation, I planned to first examine whether preconditions for testing mediation were in place; these include the presence of associations between the predictor and the outcome variable, the predictor and the hypothesized mediator, and the hypothesized mediator and the outcome variable, controlling for the effects of the predictor (Baron & Kenney, 1986). Therefore, mediation analyses were planned only in cases where associations were found between a predictor (i.e., stress, parent history of depression, parenting, temperament, genetic polymorphisms) and cortisol classes or AUC<sub>g</sub> (i.e., the mediator), and between cortisol class membership or AUC<sub>g</sub> with depressive symptoms at follow-up. Evidence for mediation exists

when the direct path between the predictor and the outcome is reduced when the hypothesized mediator is included in models (Baron & Kenney, 1986).

Mediation can be tested using the bootstrap sampling procedure and companion macro developed by Preacher and Hayes (2004, 2008). This procedure yields estimates of mean direct ( $c$ ) and indirect (i.e. mediated,  $c'$ ) effects and confidence intervals (CIs) derived from multiple samples. When estimated 95% CIs yielded by the bootstrapping procedure contain the value “zero” within them, the estimated effect is not statistically significant at  $p$  value less than 0.05.

### Results

Correlations between all major study variables are in Table 1. Paternal depression was positively correlated with children’s cortisol at baseline, ten-, and twenty- minute cortisol post-TSST-C and  $AUC_g$ . Paternal depression was also significantly correlated with child depressive symptoms at follow-up. Maternal depression was negatively correlated with observed positive parenting and 5-HTTLPR, such that those with a history of maternal depression were more likely to be homozygous or heterozygous for the  $s$  allele. Maternal history of depression was not correlated with child depressive symptoms at baseline or follow-up. Positive parenting was positively associated with family income. Observed negative parenting was negatively correlated with child PE observed during the Lab-TAB. Child PE was also negatively correlated with child BI observed during the Lab-TAB and  $AUC_g$ . Child BI was significantly positively correlated with cortisol at baseline, 0-, 10-, 20-, and 30- minutes post TSST-C and  $AUC_g$ . Child EC was positively associated with child sex, such that girls had higher EC. Child EC was also negatively correlated with depressive symptoms at follow-up. 5-HTTLPR was positively correlated with baseline cortisol, such that children with one or two copies of the  $s$  allele had higher baseline cortisol levels. Child sex was negatively correlated with child depressive symptoms at follow-up;

boys reported more depressive symptoms at follow-up than girls. Child  $AUC_g$  was positively correlated with depressive symptoms at baseline. Finally, child depressive symptoms at baseline and follow-up were positively correlated.

### **Latent Class Growth Analysis (LCGA)**

Several criteria were used to test model fit of LCGA models. As other studies examining classes of reactivity have previously identified three- and four-class solutions relevant to depressive disorders (Hankin et al., 2010; Ji, Negriff, Hansung, & Susman, 2016; Koss, George, Davies, Cicchetti, Cummings, & Sturge-Apple, 2013; Luby et al., 2003), I examined solutions for one- through four-classes using multivariate nonlinear models (i.e., including intercept, linear slope, and quadratic slope). The Bayesian Information Criterion (BIC) statistic was used; a solution with  $k$  classes should be lower than for a solution with  $k-1$  classes, in which case additional classes represent improved model fit (Jung & Wickrama, 2008). Entropy, a standardized summary measure of the classification accuracy based on posterior probabilities, was also examined. Entropy values range from .00 to 1.00, with higher values representing more accurate classification (Jung & Wickrama, 2008). The bootstrapped Lo, Mendell, and Rubin test (BLRT; Nylund, Asparouhov, & Muthén, 2007) which compares the improvement of fit between neighbouring class solutions was also used to evaluate model fit. The BLRT provides a  $p$  value that can be used to determine if there is a statistically significant improvement in fit by the inclusion of an additional class. Finally, I evaluated the substantive usefulness of classes (Muthén, 2004; Luyckx, Schwartz, Goossens, Soenens, & Beyers, 2008). If a solution with  $k$  classes emerged in which additional classes were slight variations of other, similar classes, and therefore did not add substantive meaning, the more parsimonious solution with  $k-1$  classes was chosen. Selection criteria for each class solution can be found in *Table 2*.

Class models are shown in *Figure 3*. The one-class solution shows the unconditional model. Overall, children demonstrated the expected quadratic curve showing increase in cortisol from baseline to ten-minutes post-stress followed by a subsequent decline. In the two-class solution, Class 1 ( $n = 12$ ) had lower baseline cortisol levels and steadily increasing cortisol over time, with no post-stress decrease, suggesting impaired recovery of the system (i.e., an impaired recovery class). A second class, which comprised the majority of the sample ( $n = 193$ ), was characterized by an increase in cortisol post-stress followed by a recovery to baseline levels (i.e., a normative recovery class). In the three-class solution, an additional group emerged characterized by baseline levels similar to Class 2 followed by a steady decrease following the TSST-C. Finally, a four-class solution was examined in which a blunted reactivity group emerged, showing blunted baseline cortisol and reactivity across the TSST. The two-class model was found to be the best-fitting model, adjusted BIC = 248.11, entropy = .94, Lo-Mendell-Rubin adjusted LRT = 43.05,  $p = .14$ , bootstrapped LRT value = 45.07,  $p < .001$ , and as a result, this solution was used in all subsequent analyses (see *Figure 4*).

**Predictors of group membership.** Predictors of class membership (i.e., the impaired versus normative recovery classes) were analysed using Mplus software. Models were run including all predictors within the same model, as well as in models in which each predictor individually regressed on cortisol class membership. Similar findings emerged in both models. The odds ratio (OR) for each variable of interest predicting class membership is presented in *Table 3*. Neither maternal nor paternal history of depression was associated with class membership. There was a significant effect of parenting quality, such that lower negative parenting was associated with a higher probability of being in the normative recovery class; positive parenting was unrelated to class membership. Child BI was not associated with class

membership, while PE was at a trend level; higher PE was associated with a higher probability of being in the normative recovery class than the impaired recovery class. Child EC was also associated with class membership, with children lower in EC more likely to be in the normative recovery class than the impaired recovery class. Stressful life events were unrelated to cortisol class membership. Finally, associations were examined between child genotype and cortisol class membership. No significant effects emerged for 5-HTTLPR genotype and child cortisol classes; however, DRD4 genotype was significantly associated with cortisol class membership: children in the normative recovery class were less likely to have a copy of the 7-repeat allele compared to children in the impaired recovery class.

### **Mediation Analyses**

Mediation analyses were intended as the next step, conducted to examine whether markers of child cortisol (i.e.,  $AUC_g$  and class membership) mediated associations between risk factors (e.g., parent history of depression, temperament, etc.) and child depressive symptoms at follow-up. However, significant bivariate associations between predictors and the hypothesized mediators, as well as between the hypothesized mediators and the outcome, were not found. Specifically, no significant associations were found between risk factors (i.e., stressful life events, maternal depression, etc.) and cortisol function. Further, neither index of child cortisol function predicted depressive symptoms at follow-up. Thus, full mediation analyses were not conducted.

### **Discussion**

I examined whether distinct patterns of cortisol reactivity could be identified following a psychosocial stress task in middle childhood. I also tested whether well-established predictors of depression (e.g., parent history of depression, temperament, genetics; Caspi et al., 2003; Durbin,

et al, 2005; Hammen et al., 2004; Klein et al., 2002; Morris et al., 2004) were associated with children's cortisol class membership. Finally, I planned to examine whether cortisol classes and  $AUC_g$  mediated associations between risk factors and future depressive symptoms in late childhood, although these analyses were not conducted as relations between relevant variables did not meet the preconditions for testing mediation. To my knowledge, this study is the first to examine these questions using a multimethod, longitudinal design. The present work provides new information regarding children's profiles of cortisol reactivity and recovery in middle childhood, as well as predictors of these profiles.

Overall, my findings indicate that distinct patterns of reactivity identified following stress are meaningfully related to well-established predictors of risk for internalizing disorder. Although cortisol classes did not predict future depressive symptoms, class membership was differentially associated with various well-established risk factors for depressive disorders. Specifically, I found low child PE, greater negative parenting, presence of the DRD4 7-repeat allele and high EC predicted impaired cortisol recovery following the TSST-C.

As base rates for depressive disorders are generally lower in childhood (Costello, Copeland, & Angold, 2011), significant associations between cortisol and depressive symptoms may not have been identified due to the young age and reduced variance in depressive symptoms of the children at follow-up (age 12). One avenue that may prove fruitful in this age group, given the low levels of depressive symptoms, would be to identify associations between cortisol function and other potential mediators of depression risk. For example, future research should test whether risk factors (i.e., parental depression) predict differences in cortisol reactivity which influences mechanistic variables (e.g., cognitive vulnerability) which then in turn influence depression risk. Additionally, it is possible that cortisol function may be related to disorders



more common in middle-to-late childhood (e.g., certain anxiety disorders) not examined in the current study. Given the high heterotypic continuity between anxiety and depression (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), it could be that anxiety is more proximally related to children's cortisol reactivity to stress than depression in this age group.

### **Assessing Clusters of Cortisol Reactivity.**

LGCA models were run for 1-4 classes (see *Figure 3*). Although I did not find support for the three-class model sometimes reported in the literature (i.e., average, hypo- and hyper-reactive reactivity profiles; Badanes, Watamura, & Hankin, 2011; Rao, Hammen, Ortiz, Chen, & Poland, 2008; Stetler, & Miller, 2011), the two-class model I found showed similarities to previously published work by Ji and colleagues (2016), with some notable differences. A moderate response group identified by Ji et al. showed a profile similar to the normative recovery group in the current sample, with an increase in cortisol in response to the TSST-C followed by a return to baseline levels. The impaired recovery class in the current sample showed a prolonged cortisol response with no evidence of recovery, similar to the increasing cortisol group identified by Ji et al.; however, the impaired recovery class in the current sample showed relatively low baseline levels rather than heightened baseline cortisol, as found in the Ji et al. sample. It is worth noting that Ji and colleagues obtained two baseline samples prior to the TSST-C (25- minutes and 5-minutes prior to the TSST-C). It is possible that the heightened baseline levels found in the Ji et al. studies reflected reactivity to the laboratory assessment (Gunnar & Talge, 2008). In the current study, considerable efforts were made to obtain an accurate estimate of baseline cortisol; children spent 30 minutes prior to the TSST-C to acclimatize to the lab environment, playing quietly or reading in one of the laboratory rooms. This acclimatization period prior to collecting

baseline samples may account for the relatively lower baseline cortisol levels in the current study.

The impaired recovery class in the current study also showed some overlap with a profile identified in children in response to a parent conflict stress task (Koss et al., 2013). Koss and colleagues found that a recovery profile similar to one in our sample was associated with a history of child-related conflict, perceived threat, and children's emotional insecurity. Children in the increasing group also displayed the highest rates of concurrent and subsequent internalizing and externalizing problems. This suggests these classes of cortisol reactivity may represent distinct groups that are differentially implicated in risk for depressive disorders.

Of note, all of these studies discussed examined classes of cortisol reactivity in community samples of children across middle- to late-childhood. The differences in stress tasks used, number of samples collected pre- and post-stress, and components modeled (intercept, slope and quadratic curvature) may have contributed to the mixed findings across studies. However, a pattern of cortisol function similar to the impaired recovery class in the current study, steadily increasing and no recovery, was noted across all three studies and identified as a response profile that may capture children risk for depressive disorders.

### **Predictors of Class Membership**

I predicted that well-established predictors of depressive symptoms would be meaningfully related to classes of cortisol reactivity following the TSST-C. Partial support for this hypothesis was found. With respect to child temperament, PE was associated with cortisol class membership at a trend level, with the impaired recovery class showing lower PE than the normative recovery class. This finding is consistent with previous studies finding that low PE is associated with depressive symptoms (Clark, 2005) in that cortisol function may mark risk for

future depressive symptoms. Given studies showing high PE may buffer associations between risk factors and stress (Mackrell et al., 2014), examining associations between PE and other risks in larger samples may show whether PE serves as a moderator of various risks for depression and of cortisol function as well the role of PE in predicting class membership.

Child EC was associated with cortisol class membership; children in the impaired recovery class had higher EC compared to children in the normative recovery class. This is of interest given that previously reported associations between EC and child cortisol are mixed. For example, Mayer and colleagues (2014) observed differences in the pattern of associations between EC and cortisol depending on the type of stress task used: In this study, lower EC was associated with greater cortisol response (steeper reactivity slopes) to a frustration-eliciting stressor while the reverse pattern was found in the context of a fear-evoking stress paradigm, similar to the pattern observed in the current study. Similarly, mixed associations have been found with respect to EC and depressive symptoms, with studies linking both low (Eisenberg et al., 2009; Kotelnikova et al., 2014; Oldehinkel et al., 2007) and high EC to internalizing risk (Murray & Kochanska, 2002). This variability may be partially due to differences in how EC is conceptualized; Eisenberg and colleagues (2009) noted that EC can be broken down into facets related to attentional control (e.g., attentional focus and shifting) as well as the ability to inhibit dominant responses or initiate behaviours based on social norms (e.g., inhibitory control). In the current study, EC was conceptualized as aspects of inhibitory control, derived from observed child compliance and impulsivity (Kotelnikova et al., 2014). Of note, studies examining associations between child cortisol and inhibitory control and related constructs tend to find lower inhibitory control to be associated with greater cortisol reactivity (e.g., Finy et al., 2014; Spinrad et al., 2009). Thus, when comparing across studies of child EC and cortisol, it may be

particularly important to consider differences in how EC is conceptualized as it may account for variation across studies.

No significant associations were found between child BI and class membership. This was surprising given that research on child temperament and cortisol generally finds positive associations between child BI and children's cortisol (Hastings & Utendale, 2008). However, most studies that have identified associations between BI and cortisol have focused on baseline cortisol or CAR rather than classes of reactivity (e.g., Buss et al., 2003; Fox et al., 2005) and have tested associations in younger children, reducing the comparability of our findings to these other studies. Also, the majority of studies testing associations between BI and cortisol reactivity in early and middle childhood have relied on fear and frustration paradigms (e.g., Schmidt & Fox, 1998) as opposed to psychosocial stress tasks such as the one used in the current study. The development of comparable, developmentally appropriate stress tasks is needed in order to characterize the stress response over time as well as to identify risk factors relevant to cortisol function and change in cortisol reactivity and depression risk over time.

Associations between child genotype (i.e., 5-HTTLPR and DRD4) and class membership were also tested. While no significant associations were found between 5-HTTLPR and class membership, children in the normative recovery class were less likely to have a copy of the 7-repeat allele compared to children in the impaired recovery class. Past studies of DRD4 and cortisol have linked the DRD4 7-repeat allele with an attenuated cortisol response (Buchmann et al., 2014). While the impaired recovery class in our sample showed a similar pattern of blunted baseline levels to that reported in previous studies (Buchmann et al., 2014), children in the current study also showed a failure to recover post-stress, which is not always found in other samples (Armbruster et al., 2009). Of note, other studies examining reactivity to the TSST and

associations with DRD4 have used different analysis techniques (e.g., ANOVA), and examined associations between DRD4 and cortisol in young adults rather than children (Ambruster et al., 2009; Buchmann et al., 2014). Future replication in a larger sample is necessary; however, this suggests the need to further explore associations between DRD4 and cortisol in children. It is important to note that our sample size was small for testing genetic effects, particularly in smaller groups, so replication of these findings is necessary. Sample size considerations also prevented me from testing interactions between DRD4 and other risks. Given the literature finding evidence for DRD4 as a moderator of other risks (Bachmann et al., 2014), examining if DRD4 genotype-cortisol associations are moderated by other risks may prove useful.

Parent history of depression also did not predict cortisol class membership. This finding was somewhat surprising given the growing body of literature linking parents' depression history to children's cortisol and mental health (Mackrell et al., 2014; Ramchandani, 2005). It is worth noting that most studies linking parent depression history to children's cortisol have focused on associations with CAR, AUC, or have examined reactivity to stress of samples as a whole using multi-level modelling analyses (Halligan, Herbert, Goodyear & Murray, 2004; Laurent et al., 2013) rather than predicting subclasses of reactivity, as I did in the current study.

Significant associations between parenting style and children's cortisol class membership were found, such that children in the impaired recovery class (i.e., those who showed steadily increasing cortisol levels and no recovery) were more likely to be exposed to greater negative parenting compared to children in the normative recovery class. I did not find a significant effect for positive parenting; however, it may be that positive parenting serves as a moderating factor, buffering the effects of vulnerabilities (e.g., temperamental, stressful life events) rather than direct predictor of children's cortisol. Consistent with this idea, Hagan and colleagues (2011)

found positive parenting moderated associations between negative life events on children's cortisol such that children who experienced greater positive parenting were less reactive than children who experienced lower positive parenting. Future research testing interactions between positive parenting and predictors of cortisol reactivity is needed to determine if positive parenting moderates the effects of other factors associated with children's cortisol.

Surprisingly, stressful life events were not associated with children's cortisol class membership. Although unexpected, this is consistent with the relatively weaker associations found between risk factors and outcomes in early and middle childhood as compared to those typically identified in studies of adolescents and adults (Abela & Hankin, 2008). It may be that the relationship between life stress and cortisol is moderated by other factors (e.g., temperament, parenting) at this time point. Interactions between predictors were not tested in the current study as the sample size of the impaired recovery group was modest ( $N = 12$ ). However, associations between stressful life events and children's cortisol reactivity may be intensified in the presence of other known risks (e.g., parent depression, poor parenting, genetic risk). It is also important to note that data from the current study come from a community sample that is likely exposed to less severe forms of stressful life events. Future replication of this study in a high-risk sample would allow for more fine grained tests to determine if the quality of stressful life events is differentially related to children's cortisol. This would be consistent with previous studies (Hammen, 2005; Harkness, Stewart, Wynne-Edwards, 2011) which have found differences in associations between cortisol and stress depending on the quality and intensity of stress. Associations between stressful life events and children's cortisol in adolescence should be examined, when children tend to be exposed to greater stress (Rudolph & Hammen, 1999). Finally, the absence of main effects of stressful life events may be due to the nature of our

assessment of stressful life events, specifically, the use of questionnaire methods. Future follow-ups using interview methods, considered the gold standard for assessing life stress (Monroe, 2008), are important to determine if associations may emerge when using more rigorous methods to assess the associations between stress and cortisol reactivity during middle and late childhood.

### **Mediation Analysis.**

I also predicted that cortisol would serve as a mediator of associations between known risks for depression (e.g., parent history of depression, life stress, etc.) and child depressive symptoms. However, I did not find support for mediation in the current study; specifically, relationships between key study constructs did not satisfy preconditions for mediation; nonsignificant associations were found between predictors (e.g., parent history of depression, temperament, etc.) and cortisol, predictors and depressive symptoms or cortisol and depressive symptoms. Of note, one of the few studies testing cortisol as a mediator of future risk also failed to find significant effects. Tse and Bond (2004) for example found no evidence for cortisol mediating associations between social support and depressive symptoms, instead finding evidence for social support as a mediator of links between cortisol and future depressive symptoms. This suggests that cortisol may be mediated by, rather than serve as a mediator of, other known risks for depression.

I also did not find any direct associations between child cortisol (both  $AUC_g$  and cortisol classes) and children's future depressive symptoms. This may be due to the low-risk nature of the sample used; models were tested in a community sample of children ages 11-12 at follow-up. Mean DSRS symptoms in the sample at follow-up were relatively low ( $M = 9.19$ ) in comparison to those considered at clinical range (clinical cut-off = 17). Thus, the limited variance in depressive symptoms limited my ability to detect mediated effects. Future research testing these

models in older children and clinical populations may be more likely to find evidence for mediation in children with greater variation in both depressive symptoms and in predictors of risk (i.e., stressful life events, parent history of depression).

Given the pattern of findings emerging between significant predictors and cortisol in the current sample, future work should examine moderated mediation models. Multiple risk factors were found to predict cortisol in the current study (i.e., PE, EC, negative parenting, DRD4). Of note, all of the variables found to predict cortisol in the current study have also been identified as those which either moderate, or are moderated by, other known risks associated with the cortisol response (Armbruster et al., 2009; Hagan et al., 2011; Kryski et al., 2013; Mackrell et al., 2013). Thus, tests of moderated mediation may identify further associations not detected in the current study. Due to the number of predictors already included in models, I did not test moderated mediation in the current study.

### **Strengths, Limitations and Future Research**

This study had a number of strengths, including the use of structured clinical interviews to assess parent history of depression, prospective, observational measures of child temperament, relatively low attrition, and the use of a laboratory stress task. Steps were taken to maximize the likelihood that I would obtain an accurate baseline measure of children's cortisol and multiple samples of cortisol were obtained post-stress. This is also one of few studies examining classes of cortisol reactivity in middle childhood which has been noted as an important developmental period prior to notable increases in depression. This study also included measures of both maternal and paternal depression history. In community samples such as that used in the current study, it is important to consider the impacts of fathers' mental health on child outcomes as they are more likely to share childrearing duties.



This study also had some important limitations. First, I did not have a measure of child cortisol at the baseline assessment, when children were seven-years-old. As a result, it is not clear if child temperament, genetics and negative parenting shaped classes of cortisol reactivity in a causal manner, or if these associations already existed at baseline, which would be consistent with reverse causality. Second, the relatively smaller number of children in Class 1 may have reduced my ability to detect main effects, and interactions predicting cortisol classes were not tested for this reason as well. I also did not have measures of child cortisol at later follow-ups, preventing me from testing change in class membership over time. Future studies collecting cortisol at multiple follow-ups are also needed to examine stability and predictors of cortisol class membership over time. The development and use of comparable stress tasks over time is also needed in order to characterize changes in the stress response over time and how stability or change of cortisol profiles may relate to depression risk. As previously mentioned, in younger children stress tasks use typically consist of fear and frustration paradigms, which are not directly comparable to socially-evaluative stress tasks such as the TSST typically used with older children, adolescents and adults (Dickerson & Kemeny, 2004; Gunnar, Talge, & Herrera, 2009; Lopez-Duran, Hajal, Olson, Felt, & Vazquez, 2009).

Although the use of a community sample is, in many respects, a strength of the current study, the limited number of fathers with a history of depression limited my ability to examine more fine-grained effects of parent depression on child cortisol function (e.g., timing of parental depression). Future studies using high risk samples or oversampling for parent depression are needed to determine if parental depression predicts cortisol class membership, as well as to allow tests of potential mechanisms by which parental depression may influence child cortisol function. Similarly, the use of a community sample may have reduced the number or severity of

stressful life events, which may have limited the ability to detect associations with child cortisol. Future studies testing similar models in high-risk samples using interview methods of stressful life events will be better equipped to determine whether life stress predicts cortisol class membership. I also included multiple variables in models predicting cortisol class membership and their associations with child cortisol reactivity. Although such an approach increases the likelihood of Type I error, I did not want to apply overly stringent corrections to hypothesis testing which may have limited my ability to detect potentially important effects.

This study represents an important contribution to the limited literature on associations between meaningful predictors of depression risk and children's cortisol. I identified two distinct classes of cortisol reactivity in response to a structured laboratory stress task. These were differentially related to multiple well-established correlates of depression (i.e., negative parenting, child temperament, genetic risk). Future research extending the current findings in a larger sample allowing for the exploration of potential moderation between risks in their prediction of cortisol class membership and testing moderated mediation models predicting future depressive symptoms in adolescence are needed. Given the absence of main effects for some well-established risk factors and child cortisol (e.g., parent history of depression, stressful life events) it would be of interest to determine if the associations between these variables and cortisol may emerge in the presence of other risks. Overall, this study highlights the importance of considering the data analysis method used when comparing findings across studies of child cortisol in middle-to-late childhood. Additionally, this study demonstrates the value of examining separate patterns of reactivity within a sample which may be meaningfully related to future risk for disorder and may serve as a means of identifying children at risk and providing more targeted early interventions.

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Table 1. Correlations among study variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.Life Stress	--																			
2.Father Depression	.01	--																		
3. Mother Depression	-.09	.14	--																	
4. Positive Parenting	.06	-.01	-.22**	--																
5. Negative Parenting	.06	-.03	.12 <sup>†</sup>	.07	--															
6. PE	-.02	.03	-.02	-.04	-.20**	--														
7. BI	.05	.04	.06	-.01	.10	-.15*	--													
8. EC	.05	.01	.00	.10	-.15*	-.61*	.15*	--												
9. 5-HTTLPR	.10	.01	-.17*	-.08	.02	-.03	-.04	.07	--											
10. DRD4	-.03	.02	.09	-.01	.05	.09	-.11	.04	-.03	--										
11. Sex	-.07	-.01	.05	-.02	.08	-.06	.08	.21**	.04	.00	--									
12. Family Income	.12	-.08	-.10	.29**	.02	-.07	.00	.09	.00	.09	-.03	--								
13. Baseline cortisol	.05	.24**	-.06	.03	-.07	-.03	.18*	.01	.19*	.02	-.04	-.10	--							
14. Zero min cortisol	.15 <sup>†</sup>	.11	-.04	.08	.12	-.15 <sup>†</sup>	.26**	.03	.10	.00	-.03	-.09	.63**	--						
15. Ten min cortisol	.04	.22**	.03	.04	.14 <sup>†</sup>	-.17*	.22**	.10	-.04	.05	-.11	-.01	.38**	.62**	--					

16. Twenty min cortisol	-.01	.19*	.03	.02	.09	-.15 <sup>†</sup>	.29**	.08	-.03	.03	-.10	.02	.36**	.56**	.79**	--				
17. Thirty min cortisol	-.03	.08	.05	-.05	-.03	-.10	.27**	.07	-.03	-.10	-.10	-.04	.32**	.44**	.61**	.80**	--			
18. AUC ground	.06	.21**	.01	.04	.10	-.17*	.30**	.08	.02	-.04	-.10	-.04	-.26**	.81**	.91**	.90**	.76**	--		
19. DSRS T1	-.04	.09	.09	-.10	-.07	.04	-.05	-.04	-.05	.13	-.10	.02	.04	-.11	-.15	-.08	-.16*	-.19*	--	
20. DSRS T3	-.12	.16*	.08	-.04	-.10	.12 <sup>†</sup>	-.14*	-	-.03	.04	-.16*	-.10	-.02	-.13	-.06	-.08	-.18*	-.11	.40**	--
MEAN	.00	--	--	.01	.00	.00	.00	.00	--	--	--	3.63	.03	.04	.05	.04	.03	.16	12.93	9.19
SD	.72	--	--	3.60	1.38	3.89	.64	1.69	--	--	--	1.18	.02	.03	.03	.03	.03	.09	5.48	4.19

\*\*  $p < .01$ , \*  $p < .05$ , <sup>†</sup>  $p < .10$

Note: for child sex, boys were coded as '0' and girls as '1', for parent depression, no parental depression was coded as "0" and a history of parent depression as "1." BI = Behavioral Inhibition; PE = Positive Emotionality; EC = Effortful Control; 5-HTTLPR = serotonin transporter gene; DRD4 = dopamine D4 receptor; AUC = Area Under the Curve; DSRS = Depression Self-Rating Scale.

Table 2. Model fit statistics for Latent Growth Class Analysis

<i>Model Fit/Classification</i>	<i>1-Class Model</i>	<i>2-Class Model</i>	<i>3-Class Model</i>	<i>4-Class Model</i>
Loglikelihood	-78.57	-89.45	-89.41	-80.41
AIC	185.13	204.91	194.82	181.56
Adjusted BIC	184.21	248.11	251.31	251.34
Entropy (range 0 to 1)		.94	.92	.93
Lo-Mendell-Rubin Adjusted LRT		43.05, $p$ =.14	17.24, $p$ =.39	11.13, $p$ = .34
Bootstrapped LRT		$p$ <.001	$p$ < .02	$p$ =.19
N in each class	C1 = 205	C1 = 12, C2 = 193	C1 = 12, C2 = 180, C3 = 12	C1 = 175, C2 =11, C3 = 4, C4 = 15

*Note:* See graphs below for 1, 2, 3, and 4-class models. Better fit is indexed by lower AIC and adjusted BIC, as well as significant LRT tests. Relative entropy is defined on [0, 1], with values near 1 indicating high certainty in classification and values near 0 indicating low certainty. 2-class model fits better than a single class-model; 3-, and 4-class models do not fit better than a 2-class model.

Table 3. Predictors of class membership.

<i>Predictor</i>	<i>Class 2 vs. Class 1</i>
Child sex	.04(.59)
Maternal history of depression	.99(.80)
Paternal history of depression	-3.15(.66)
Negative Parenting	-.45(.12)**
Positive Parenting	.03(.07)
Child PE	.11(.07)†
Child BI	.03(.43)
Child EC	-.92(.41)*
Stressful Life Events	-.36(.40)
5-HTTLPR	-.23(.67)
DRD4	-4.90 (.68)**

Note: \*\*  $p < .01$ , \*  $p < .05$ , †  $p < .10$

PE = Positive Emotionality; BI = Behavioral Inhibition; EC = Effortful Control; 5-HTTLPR = Serotonin Transporter Gene; DRD4 = Dopamine D4 Receptor Gene.

Results are for the multinomial logistic regression of the categorical latent variable  $c$  on the covariate when comparing Class 2 versus Class 1 (class 1 as reference class). Values are presented as odds ratios (SE).

Figure 1. Timeline showing Study 2 data collection.

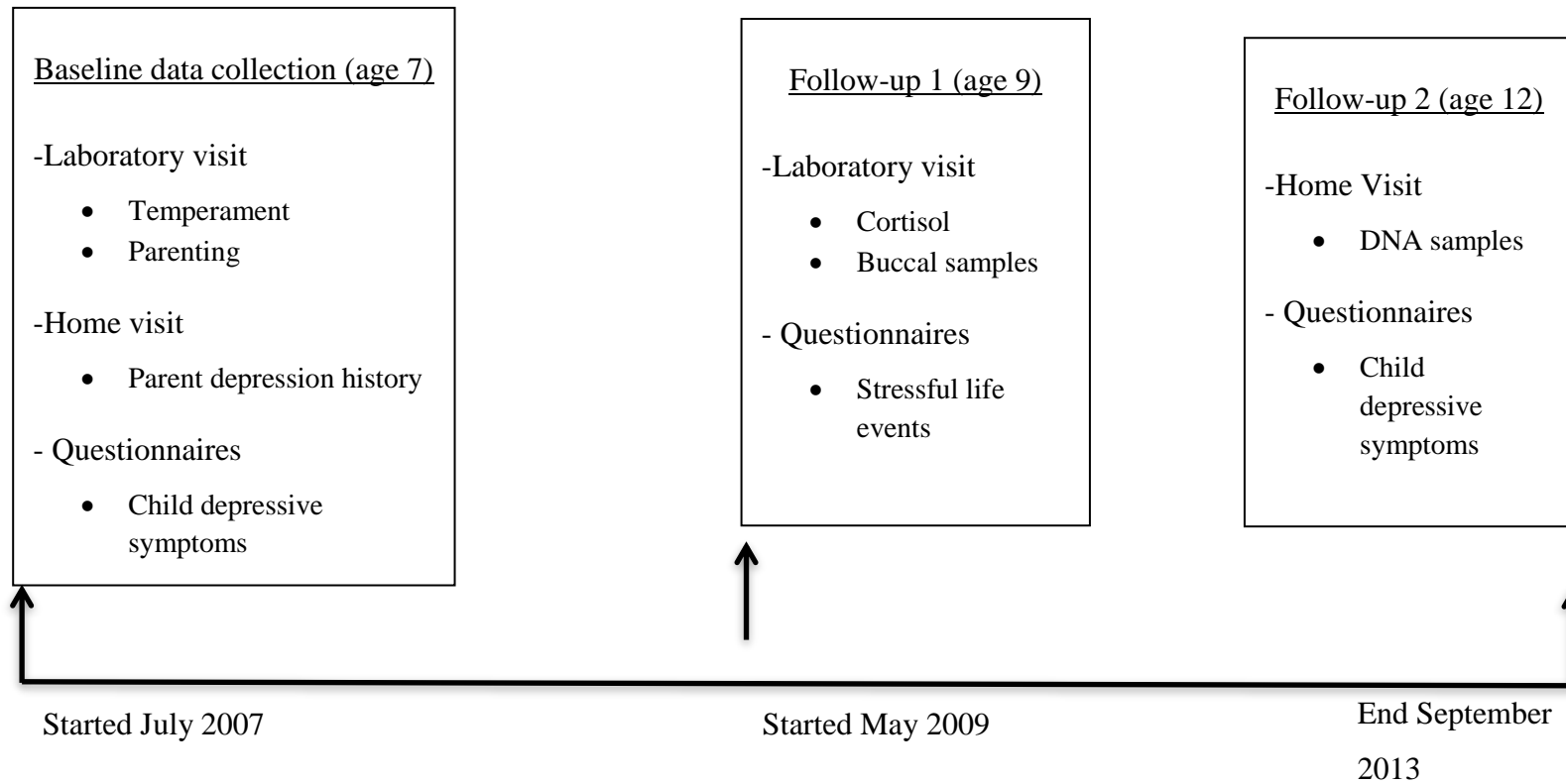


Figure 2. Hypothesized mediation model.

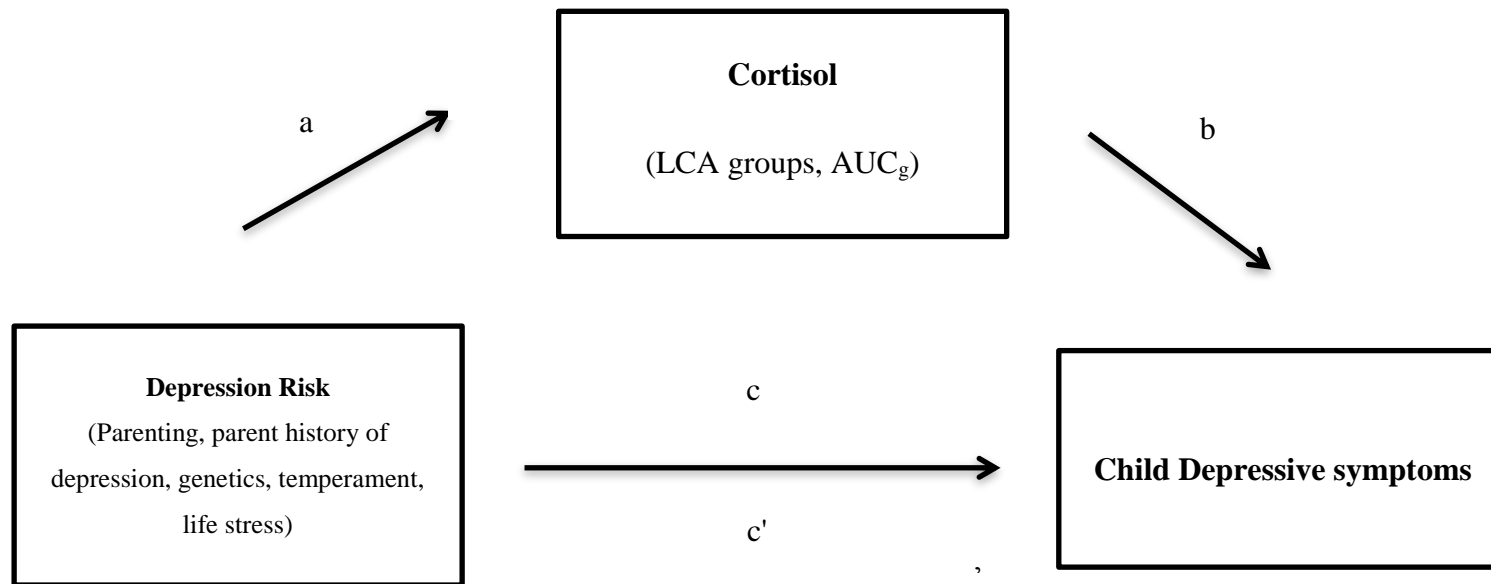


Figure 3. Latent growth class models 1-4.

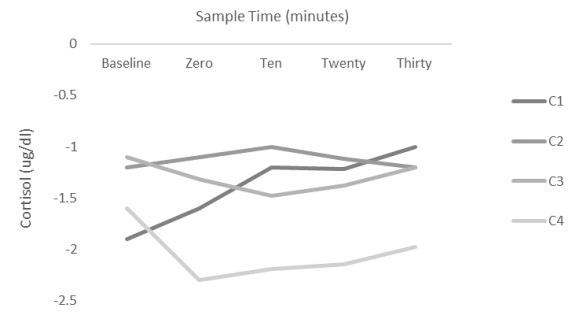
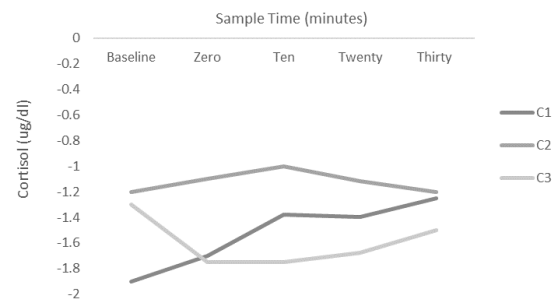
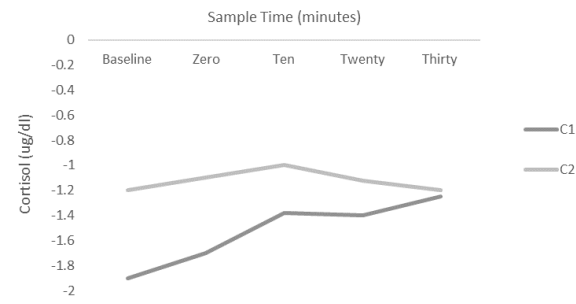
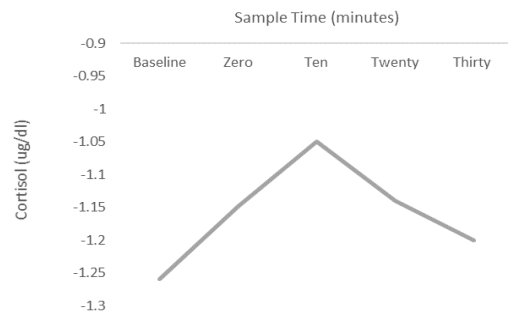
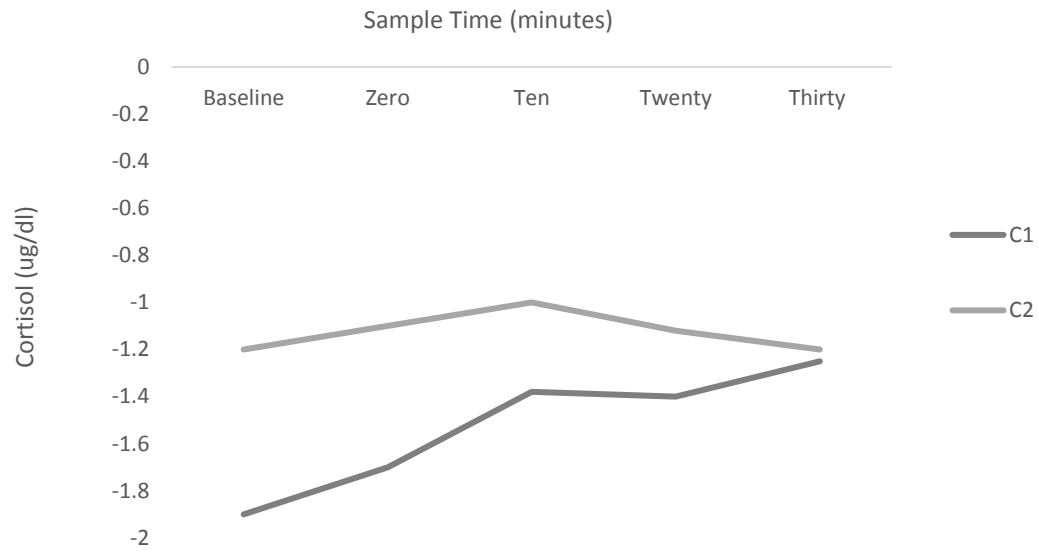




Figure 4. Two class latent growth class model used in all predictor and mediation model analyses.



Note: Class 1 N = 12, Class 2 N = 193.

## General Discussion

Del Giudice (2014) described middle childhood as a developmental “switch point” or time of heightened sensitivity to rapid changes in development. In middle childhood, rapid developmental changes are taking place cognitively, physically, socially and hormonally (McHale, Crouter, Tucker, 2001). However, in contrast to other periods in development, middle childhood remains relatively understudied. In particular, there are few existing studies using multi-method, longitudinal designs, although these are best equipped to capture the interplay between vulnerabilities that may put children at risk for developing depression (Klein, Dyson, Kujawa, & Kotov, 2012). The use of multi-method, longitudinal designs incorporating multiple risk factors is necessary for the development of targeted interventions and prevention programs to mitigate the long-term costs associated with depression across the lifespan (Cabello, Mellor-Marsá, Sabariego, Bickenbach, & Ayuso-Mateos, 2012; Cicchetti & Toth, 1999; Satyanarayana, Enns, Cox, & Sareen, 2009). Additionally, these designs are needed to establish temporal relationships between various risk factors (i.e., parental depression, stressful life events) contributing to the onset and maintenance of symptoms across time. In particular, the use of longitudinal studies incorporating questionnaire, laboratory based tasks, and psychophysiological measures would allow for a comprehensive picture of both potential risk and protective factors at crucial stages of development prior to the rapid increase in rates for depressive disorders in adolescence (Klein et al., 2012). The current two studies addressed some of these gaps in the literature, examining associations between known risks for depressive disorders and depressive symptoms over middle-to-late childhood, incorporating laboratory, psychophysiological measures, and multiple-informant reports.

Although there has been a growing body of literature testing predictors of depression in childhood, studies have generally focused on a limited number of narrowly defined risks. This

tendency to study risks in isolation is problematic as it prevents the investigation of possible additive, interactive, or mediating effects between risks associated with depression (Hammen, Shih, & Brennan, 2004; Kryski, 2014). One consistent finding with respect to depression risk in middle-to-late childhood is relatively weak or inconsistent findings between predictors and symptoms compared to those reported for adolescents and adults (Abela & Hankin, 2008). One possible explanation for this pattern is that effects of various risk factors in their association with depression are amplified in the context of changes associated with puberty. Consistent with this hypothesis, in Study 1 I found evidence that the effects of some common risks (i.e., stressful life events, parental depression) were moderated by pubertal development such that risk factors in the context of greater pubertal development predicted depressive symptoms in children at follow-up. This finding suggests that in middle and late childhood, effects of commonly identified risks may have weaker effects prior to the onset of puberty and be intensified by changes associated with pubertal development. This proposal fits within a diathesis-stress context in which changes associated with puberty may serve as a stressor which may interact with other risks increasing the risk for future depressive symptoms (Abela & Sullivan, 2003; Hankin, Abramson & Siler, 2001).

Of note, children in the current study were nine-years-old when pubertal status was assessed. In contrast, studies of pubertal development have typically focused on children in the range of 12-15 years (Angold, Costello, & Worthman, 1998). Given that on average pubertal development begins between the ages of 9.5 and 12 years (Downing & Bellis, 2009), the effects of puberty on risk for depression may emerge earlier than typically studied. This suggests a need not only to increase the number of studies incorporating multiple predictors to investigate

moderating influences of various risks such as puberty in association with depression, but also, to study these factors in earlier in development.

I chose to focus on pubertal development in with respect to total number of pubertal features reported (e.g., growth in height, presence of bodily hair, menarche). Another related construct associated with depression risk, in particular with respect to gender differences, is pubertal timing. Pubertal timing reflects not only the presence of pubertal features, but also, the relative timing of these changes compared to one's peers (Angold, Costello, & Worthman, 1998). Although sex differences were not a focus of Study 1, I tested whether sex differences were present in preliminary analyses and found no significant interaction between pubertal status and child sex (all  $ps > .10$ ). This was not surprising given the relatively young age of children in the current study compared to others which typically report sex differences (Nolen-Hoeksema & Girgus, 1994). In addition, pubertal status is less often associated with sex differences in contrast to pubertal timing (Graber, 2013). The general consensus with respect to pubertal timing research is that early-onset puberty for girls (Galvao, Silva, Zimmerman, Martins, & Pereira, 2014; Hamilton, Hamlat, Stange, Abramson, & Alloy, 2014) and late-onset puberty for boys (though this finding is somewhat less consistent; Mendle & Ferrero, 2012) is associated with depression risk. The measure used to assess pubertal development in the current sample was not developed for the purpose of assessing pubertal timing and was therefore this was not examined in Study 1. Additionally, I did not have the sample size to extend the current analyses to investigate risk (i.e., parental depression, stressful life events) x puberty x sex interactions. However, future studies should attempt to replicate the findings of Study 1 with older children incorporating child sex in larger samples in order to determine if three-way interactions between risk, puberty, and child sex emerge.

Future research on child pubertal development and depression risk incorporating child sex should also test interactions between child sex, pubertal status, known risks for depression (i.e., parent depression, stressful life events) and parent sex. A growing literature has suggested gendered effects of parent depression history and parenting style on boys' versus girls' mental health (Ramchandani, Stein, Evans, & O'Connor, 2005; Russell & Saebel, 1997); greater associations have been reported for mother-daughter and father-son dyads as compared to mother-son and father-daughter dyads (Landman-Peeters, Ormel, Van Sonderen, Den Boer, Minderaa, & Hartman, 2008; Ramchandani et al., 2005). Thus, boys' and girls' risk for depression may be differentially related to fathers' and mothers' depression history and parenting style. If parental depression history differs in how it relates to child risk as a function of child sex, this may also account for mixed findings with respect to strength of associations found across studies in middle childhood.

Similar to the variability in findings reported over middle and late childhood with respect to predictors of child depression symptoms, mixed findings have also been reported during this developmental period with respect to cortisol reactivity profiles implicated in depression risk. In particular, both cortisol hypo- and hyper-reactive profiles, indexed via salivary cortisol, have been associated with depression risk in childhood (Badanes, Watamura, & Hankin, 2011; Pariante & Lightman, 2008; Rao, Hammen, Ortiz, Chen, & Poland, 2008). Several methodological differences exist across current studies on this topic including variations in child age, stress task, predictors of cortisol reactivity, and method of analyzing cortisol data making direct comparisons across studies difficult (Badanes, Watamura, & Hankin, 2011; Burke, Davis, Otte, & Mohr, 2005; Gunnar, Talge, & Herrera, 2009; Lopez-Duran, Hajal, Olson, Felt, & Vazquez, 2009). As discussed in Study 2, there have been few studies to date that have examined

within sample differences in reactivity to psychological stress tasks. This is an important gap in knowledge and represents an important contribution of Study 2 to the literature on child cortisol function at this developmental period. This is particularly relevant given heterogeneity within individuals with depression (Chen, Eaton, Gallo, & Nestadt, 2000). It is likely that differences in the manifestation of symptoms across individuals with depression may be associated with a range of risk factors and be reflected in differences in cortisol reactivity profiles in response to stress. In Study 2, I found two unique classes of reactivity profiles in response to a psychosocial stress task (i.e., normative and impaired recovery). Of particular interest, these classes were differentially associated with markers of depression risk. Specifically, low PE, high EC, negative parenting, and presence of the DRD4 7-repeat allele predicted cortisol class membership. Surprisingly, I did not find associations between cortisol class membership and child depressive symptoms, potentially due to low variance in depressive symptoms at follow up; however, my findings suggest that reactivity profiles related to different risk factors associated with depression may reflect heterogeneity within those at risk for future depressive symptoms or disorders. Future research in this age group should extend these findings to examine whether different profiles predict intermediate risks for depression that present with greater variability in middle and late childhood (e.g., cognitive vulnerability, abnormal personality traits associated with depression risk).

Future research should also investigate the stability of cortisol reactivity patterns, and predictors of stability of class membership, over time. Although I was able to examine within-sample variability in cortisol reactivity to stress, I did not have measures of cortisol at baseline or follow-up that would have allowed for tests of the stability of class membership over time. Few studies have tested the stability of child cortisol class membership over time in a similar age

group, with the exception of one recent study (Ji, Negri, Hansung, & Susman, 2016). Ji and colleagues (2016) examined classes of cortisol reactivity in a longitudinal study of 8- to 13- year-old children and found moderate stability in class membership over time. However, the authors did not include measures of relevant predictors (e.g., stressful life events, parent depression history) that may have accounted for class membership or change over time. Future research is needed integrating these two approaches to study not only the stability of class membership, but also, factors that predict changes in reactivity profiles and how these profiles relate to future depression risk. The development of developmentally appropriate downward and upward extensions of currently used stress tasks to elicit cortisol reactivity is needed in order for these studies to be conducted. As discussed in Study 2, current methods of eliciting cortisol responses in young children rely primarily on fear and frustration paradigms (Lopez-Duran et al., 2009) which are not directly comparable to socially evaluative stressors typically used with adolescents and adults (Dickerson & Kemeny, 2004). Few exceptions (e.g., Kryski, Smith, Sheikh, Singh, & Hayden, 2011) currently allow for within-sample comparisons over time in youth which map on to Trier Social Stress Task which is currently the gold standard for eliciting cortisol reactivity in middle childhood, adolescents, and adults (Dickerson & Kemeny, 2004).

Although I did not find evidence for mediation in the current study, moderated mediation may also be important to models of the association between known risks, cortisol, and future depressive symptoms. For example, in Study 2, I did not find main effects for some variables (e.g., stressful life events) which have frequently been associated with cortisol reactivity in adult literature (Burke, Davis, Otte, & Mohr, 2005). Given the absence of main effects, but significant moderated effects observed in Study 1, it is possible that associations between risks and cortisol profiles may emerge in the context of other variables (e.g., pubertal development). Also of note,

some variables found to predict cortisol class membership in Study 2 (e.g., child PE, child EC, negative parenting) have previously been found to moderate other risks (e.g., parent history of depression), both buffering and exacerbating risk in some cases (e.g., Mackrell et al., 2014; McLeod, Weisz, & Wood, 2007; Morris, Silk, Steinberg, Sessa, Avenevoli, & Essex, 2004), and associations with child cortisol and depression. Thus, future studies should be done testing moderated mediation models to determine if significant associations may be identified in such models predicting future depressive symptoms. This was not done in the current sample due to the large number of predictors already included in models in Study 2.

### **Strengths and Weaknesses of Study 1 and 2**

Both studies that comprise this dissertation have important strengths. First, both studies incorporated a multi-method, multi-informant, longitudinal design. Both studies also span an important, and relatively understudied, developmental period preceding rapid increased rates in depression in adolescence. This study incorporated structured clinical interviews, observational measures of child temperament, a laboratory stress task, and had relatively low attrition. I also examined associations between depressive symptoms and child cortisol in relation to both mothers' and fathers' depression history; father depression is less frequently studied with respect to child depression and cortisol function and the inclusions of fathers in this study is an important contribution to our knowledge of fathers' depression history on child outcomes.

Study 1 and 2 also had important weaknesses to acknowledge. First, although the sample used in both studies was relatively large for one incorporating laboratory-based methods, the sample size limited my ability to conduct some analyses; in particular, tests of three-way interactions and moderated-mediation analyses were not conducted. Given the absence of main effects for some well-established risk factors and child cortisol in Study 2, it would be of interest



to determine if associations between these variables and cortisol may emerge in the presence of other risks (i.e., pubertal development) particularly given the evidence for moderation of well-established risk factors found in Study 1. I examined multiple predictors of depression risk and cortisol class membership in both studies. Although such an approach increased my likelihood of making Type I errors, I did not want to apply overly strict corrections which may have limited my ability to detect potentially important effects. Future replication is needed to confirm the effects identified in both studies in larger samples.

Although I tested predictors of depression risk and cortisol spanning multiple follow-ups, I did not specifically conduct tests of depression risk over time (i.e., multilevel modelling of change in depressive symptoms over time). While tests of stability and change in depressive symptoms over time has been done in previous studies published using the current sample (Kotelnikova, Mackrell, Jordan, & Hayden, 2014), future research should investigate change in symptoms over time incorporating the variables used in Study 1 and 2. Additionally, research incorporating measures of cortisol is needed to identify whether different profiles of cortisol reactivity emerge earlier in development and the stability of profile membership over time. I did not have a measure of child cortisol at the baseline assessment; therefore, it is not clear if parenting style, genetic polymorphisms, child PE and child EC shaped the cortisol profiles, or if these associations already existed at baseline.

Although the use of a community sample is also a strength of the current studies given the generalizability of the findings to similar samples, it also limited the number of mothers and fathers with a history of depression, limiting my ability to examine more fine-grained effects of parent depression on children's depressive symptoms and cortisol function (e.g., timing of parental depression). Future studies using high risk samples or oversampling for parent

depression are needed to determine how parental depression relates to child depressive symptoms and cortisol function, as well as to allow for tests of mechanisms by which parental depression may influence cortisol function and depression risk. The use of a community sample also may have reduced the number and severity of stressful life events, which may have limited my ability to detect direct associations between stressful life events and child depressive symptoms and cortisol function. The sample used in the current two studies was also limited in terms of demographic diversity. Participants were mostly Caucasian and were largely from middle-class families. Future research with more diverse samples is also needed. Although incorporating measures of fathers' depression was a strength of both studies, my measure of parenting in Study 2 was based on mothers' parenting quality. Future research incorporating measures of fathers' parenting are also needed. My assessment of child pubertal development would also have been improved by the addition of hormonal data which would allow me to speak more specifically to the mechanisms through which puberty may increase risk at this time (Angold, Costello, Erkanli, & Worthman, 1999; Buchanan, Eccles Becker, 1992). Future studies should incorporate hormonal data as well as self-report to identify whether differences in pubertal hormones mediate associations between risks and depression in middle and late childhood.

## **Conclusion**

Study 1 and 2 contribute to the literature on depression risk across middle-to-late childhood incorporating a multi-method, multi-informant, longitudinal design. In study 1 I found evidence for the importance of testing moderated effects during middle childhood as children are experiencing rapid changes, particularly in the context of pubertal development. During this time, many well-established predictors of risk (e.g., parent history of depression, stressful life

events) less consistently found to be associated with risk in early childhood may become strengthened in the context of changes associated with puberty. Study 2 contributed to the relatively small literature on associations between cortisol reactivity, and patterns of cortisol reactivity in middle childhood. Future work incorporating findings of both studies testing moderated mediation models would help identify a potential mechanistic role of cortisol in risk for depression. Overall, both studies highlight the importance of middle-to-late childhood with respect to future depression risk and the need for future longitudinal studies spanning this developmental period which may identify potential targets for intervention and prevention of future depressive disorders.

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## Appendix A



### Office of Research Ethics

The University of Western Ontario  
 Room 4180 Support Services Building, London, ON, Canada N6A 5C1  
 Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca  
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### Use of Human Subjects - Ethics Approval Notice

**Principal Investigator:** Dr. E.P. Hayden

**Review Number:** 12279S

**Review Date:** November 06, 2009

**Revision Number:** 14

**Review Level:** Expedited

**Protocol Title:** Child Temperament and Individual Differences in Information Processing

**Department and Institution:** Psychology, University of Western Ontario

**Sponsor:**

**Ethics Approval Date:** November 11, 2009

**Expiry Date:** June 30, 2010

**Documents Reviewed and Approved:** Revised study methodology. Letter of Information and Consent.

#### Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the applicable laws and regulations of Ontario has granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above.

This approval shall remain valid until the expiry date noted above assuming timely and acceptable responses to the NMREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the study or consent form may be initiated without prior written approval from the NMREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the NMREB:

- a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
- b) all adverse and unexpected experiences or events that are both serious and unexpected;
- c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the NMREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the NMREB.

Chair of NMREB: Dr. Jerry Paquette

Ethics Officer to Contact for Further Information			
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*This is an official document. Please retain the original in your files.*

cc: ORE File

## Appendix B



### Use of Human Participants - Ethics Approval Notice

**Principal Investigator:** Prof. Elizabeth Hayden  
**Review Number:** 12279S  
**Review Level:** Delegated  
**Approved Local Adult Participants:** 0  
**Approved Local Minor Participants:** 200  
**Protocol Title:** Child Temperament and Individual Differences in Information Processing  
**Department & Institution:** Social Science/ Psychology, University of Western Ontario  
**Sponsor:**  
**Ethics Approval Date:** March 06, 2012      **Expiry Date:** June 30, 2013

#### Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Revised Western University Protocol	An additional wave of data (Home Assessment and Parent Measures) will be collected on the children who have previously participated. The study end date has been revised to June 30, 2013.	
Revised Letter of Information & Consent		
Revised Letter of Information & Consent		

This is to notify you that The University of Western Ontario Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the applicable laws and regulations of Ontario has granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above.

This approval shall remain valid until the expiry date noted above assuming timely and acceptable responses to the NMREB's periodic requests for surveillance and monitoring information.

Members of the NMREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the NMREB.

The Chair of the NMREB is Dr. Riley Hinson. The UWO NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

For Contact for Further Information

<input checked="" type="checkbox"/> Grace Kelly (grace.kelly@uwo.ca)	<input type="checkbox"/> Janice Sutherland (jsuthor@uwo.ca)
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## Curriculum Vitae

Sarah V. M. Mackrell

### Personal Information:

Address:

Email(s):

Telephone:

### Education:

- |              |   |
|--------------|---|
| 2011-present | Doctor of Philosophy, Psychology. Personality and Measurement Program, University of Western Ontario. |
| 2009-2011    | Master of Science, Psychology. Personality and Measurement Program, University of Western Ontario.    |
| 2003-2008    | Bachelor of Science, High Distinction (Psychology). University of Toronto.                            |

### Teaching Experience:

- |      |   |
|------|---|
| 2016 | Lecturer. Psychology 2851. Statistics II for Psychology. Brescia University College.                  |
| 2016 | Lecturer. Psychology 2080 Introduction to Test Construction. University of Western Ontario.           |
| 2015 | Lecturer. Family Studies 2226A- Parenting. Brescia University College.                                |
| 2015 | Lecturer. Psychology 2035 (online)- Understanding Yourself and Others. University of Western Ontario. |
| 2015 | Advanced Teaching Program Certificate. Western University, Teaching Support Centre.                   |

- 2013-2015 Graduate Teaching Assistant. Psychology 2820- Research Methods and Statistical Analysis in Psychology. University of Western Ontario.
- 2014 Graduate Teaching Assistant. Psychology 2840- Research Methods in Psychology. King's University College.
- 2013-2014 Co-supervision of undergraduate student. UWO psychology honors program thesis based. Talia Kish.
- 2012-2013 Co-supervision of undergraduate student. UWO psychology honors program thesis based. Tamara Harduwar.
- 2013 Guest lecture, Psychology 2320B- Abnormal Child Psychology.
- 2012-2013 Graduate Teaching Assistant. Psychology 2320A/B- Abnormal Child Psychology.
- 2012 Guest lecture, Psychology 4390 Special Topics in Clinical Psychology: Personality and Developmental Psychopathology.
- 2011 Graduate Teaching Assistant. Psychology 2035- Psychological Aspects of Life-skills. University of Western Ontario.
- 2010-2011 Co-supervision of undergraduate student. UWO psychology honors program thesis based. Emily Johnson.
- 2009-2011 Graduate Teaching Assistant. Psychology 2820- Research Methods and Statistical Analysis in Psychology. University of Western Ontario.

### **Quantitative Training**

- 2014 Longitudinal Methods. Graduate course taken at the University of Western Ontario.
- 2012 International Workshop on Statistical Genetics and Methodology of Twin and Family Studies: Introductory Course.

- 2012 Structural Equation Modeling. Graduate course taken at the University of Western Ontario.
- 2011 Introduction to Structural Equation Modeling. Workshop offered by a guest instructor Dr. T. M. Olinio at the University of Western Ontario.
- 2011 Multilevel Modeling. Graduate course taken at the University of Western Ontario.
- 2010 Western Summer Institute on Longitudinal Data Analysis. Workshop offered by the Population and Life Course Studies Interdisciplinary Development Initiative and Research Data Centre at the University of Western Ontario.
- 2010 Multivariate Analysis. Graduate course taken at the University of Western Ontario.

**Academic Awards:**

- 2012-2013 Child Health Research Institute Quality of Life Initiative Graduate Assistantship (total amount: \$9500).
- 2011-2014 Ontario Mental Health Foundation Doctoral Studentship (total amount \$16 000 annually for 3 years).
- 2010-2011 Child Health Research Institute Quality of Life Initiative Graduate Assistantship (total amount: \$10 000).
- 2009-2010 Joseph-Armand Bombardier Canada Graduate Scholarship - Master's Award (SSHRC-CGS) (total amount: \$17, 500).
- 2005 - 2008 University of Toronto Honors List. Faculty of Science (total amount: \$1500).

**Travel Awards:**

- 2013 Western University Graduate Studies Travel Grant
- 2011 Behavior Genetics Association (BGA) Travel Bursary

**Membership in Professional Societies:**

- 2014-2015 Society for Research in Psychopathology
- 2011-2012 American Psychopathological Association
- 2011-2014 Behavior Genetics Association
- 2011- 2014 Canadian Psychological Association

**Publications:**

Kotelnikova, Y., LeMoult, J., **Mackrell, S.V.M.**, Sheikh, H.I., Singh, S. M., Joormann, J., Gotlib, H.I., & Hayden, E.P. (2016). The serotonin transporter promoter variant, stress, and attentional biases in middle childhood. *Personality and Individual Differences, 101*, 371-379. doi: 10.1016/j.paid.2016.06.004

**Mackrell, S. V.M.**, Kotelnikova, Y., Jordan, P., & Hayden, E.P. (2016). The role of pubertal development in emerging depression risk in middle childhood. *Personality and Individual Differences*. doi:10.1016/j.paid.2016.03.035

Hayden, E.P., Hankin, B.L., **Mackrell, S.V.M.**, Sheikh, H.I., Jordan, P.J., Dozois, D.J.A., Singh, S.M., Olin, T.M., Watamura, S.E., & Badanes, L.S. (2014). Parental depression and child cognitive vulnerability predict children's cortisol reactivity. *Development and Psychopathology, 26*, 1445-1460. Doi: 10.1017/S0954579414001138

Sheikh, H. I., Joanisse, M. F., **Mackrell, S. V. M.**, Kryski, K. R., Smith, H. J., Singh, S. M., & Hayden, E. P. (2014). Links between white matter microstructure and cortisol reactivity to stress in early childhood: Evidence for moderation by parenting. *Neuroimage Clinical, 6*, 77-85. Doi: 10.1016/j.nicl.2014.08.013

Kotelnikova, Y., **Mackrell, S. V.M.**, Jordan, P. L., & Hayden, E. P. (2015). Longitudinal

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**Mackrell, S.V.M.**, Sheikh, H.I., Kotelnikova, Y., Kryski, K.R., Jordan, P.J., Singh, S.M., & Hayden, E.P. (2014). Child temperament and parental depression predict cortisol reactivity to stress in middle childhood. *Journal of Abnormal Psychology*, *123*, 106-116. Doi: 10.1037/a0035612

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#### **Poster Presentations:**

- Mackrell, S. V. M.**, Kotelnikova, Y., Jordan, P. L., & Hayden, E. P. (2014, September). *Pubertal Status Moderates Associations Between Depression Risks and Children's Depressive Symptoms*. Poster presented at the Society for Research in Psychopathology annual meeting, Evanston, Illinois, USA.
- Kotelnikova, Y., **Mackrell, S. V. M.**, Sheikh, H. I., Singh, S. M., & Hayden, E. P. (2014, September). *The Serotonin Transporter Gene and Stress Interact to Predict Children's Attentional Biases for Positive Stimuli*. Poster presented at the Society for Research in Psychopathology annual meeting, Evanston, Illinois, USA.
- Sheikh, H. I., Joannisse, M. F., **Mackrell, S. V. M.**, Kryski, K. R., Smith, H. J., Singh, S. M., Hayden, E. P. *Hypothalamic-pituitary-adrenal axis stress reactivity is associated with differences in white matter integrity in young girls*. Poster presented at the Canada-Israel Symposium on Brain Plasticity, Learning and Education, June 14-16, London, ON, Canada.
- Mackrell, S. V. M.**, Sheikh, H. I., Kotelnikova, Y., Jordan, P. L., Singh, S. M., & Hayden, E. P. (2013, April). *Child Temperament and Parental History of Internalizing Disorders: Associations with HPA Axis Reactivity in Middle Childhood*. Poster presented at the Biennial Meeting of the Society for Research in Child Development, Seattle, Washington, USA.
- Mackrell, S. V. M.**, Sheik, H. I., Singh, S. M., Kryski, K. R., & Hayden, E. P. (2012, October). *Cognitive Vulnerability and Stressful Life Events Predicting HPA Axis Reactivity in Middle Childhood*. Poster presented at the Society for Research in Psychopathology annual meeting, Ann Arbor, Michigan, USA.
- Kotelnikova, Y., **Mackrell, S.V.M.**, Jordan, P.L., & Hayden, E.P. (2012, October). *Effortful control and cognitive vulnerability to depression in middle childhood: A multimethod, longitudinal study*. Poster presented at the Society for Research in Psychopathology annual meeting, Ann Arbor, Michigan, USA.
- Mackrell, S. V. M.**, Kotelnikova, Y., Veselka, L., Schermer, J. A., Petrides, K. V., & Vernon, P.



A. *A Behavioral Genetic Study of Sub-Clinical Personality Disorders and Trait Emotional Intelligence*. Poster presented at the Behavior Genetics Association's 41<sup>st</sup> Annual Meeting, Newport, RI, USA, June 2011.

Kotelnikova, Y., **Mackrell, S. V. M.**, Veselka, L., Schermer, J. A., & Vernon, P. A. *Non-adaptive Personality Traits and the Dark Triad: A Behavior Genetic Investigation into the Relationship between the Two Domains*. Poster presented at the Behavior Genetics Association's 41<sup>st</sup> Annual Meeting, Newport, RI, USA, June 2011.

Kotelnikova, Y, **Mackrell, S. V. M.**, Jordan, P., Hayden, E. P. (2011, May). *Temperament Traits as Predictors of Change in Internalizing Problems in Middle Childhood*. Poster presented at the Association for Psychological Science Annual Convention, Washington, DC, USA, May 2011.

**Mackrell, S. V. M.**, Schermer, J. A., Veselka, L., & Vernon, P. A. *A Behavioral Genetic Study of the Dark Triad of Personality and Moral Foundations*. Poster presented at the Canadian Psychological Association's 72nd Annual Convention, Toronto, Ontario, June 2, 2011.

**Mackrell, S. V. M.**, Jordan, P. L., Sheikh, H. I., Singh, S. M., & Hayden, E. P. *Longitudinal Associations Between Temperament, Social Adjustment and Internalizing Disorders Risk in Middle Childhood*. Poster presented at the Biennial Meeting of the Society for Research in Child Development, Montreal, Quebec, March 31, 2011.

**Mackrell, S. V. M.** *Infant Coping Behaviors following Parent's Contingent and Reinforcing Responses to Infant Imitation of Social Directed Play*. Presented at 38th Annual Ontario Psychology Undergraduate Thesis Conference held at Brock University, St. Catherine's, ON.

### **Positions of Relevance:**

2015-current

Psychometrist at Dr. Darlene Elliott-Faust and Associates.

- 2014- 2015                      Member of University of Western Ontario Department of Psychology Colloquium Committee.
- 2015                                Assistant Assistive Technologist. University of Western Ontario, Services for Students with Disabilities.
- 2014-2015                      Student Partnership Member. University of Western Ontario, Student Development Services.
- 2013- 2014                      Member of University of Western Ontario Department of Psychology Appointments Committee.
- 2009- 2011                      Member of University of Western Ontario Psychology Colloquium Committee.