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Maternal Psychosocial Distress During Pregnancy and Child Behavior Outcomes

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M.A., Emory University, 2007

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Maternal Psychosocial Distress during Pregnancy and Child Behavior Outcomes submitted to the
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Abstract

Maternal Psychosocial Distress During Pregnancy and Child Behavior Outcomes
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Background: Prenatal depression, anxiety, and stress have all been shown to be associated with adverse child behavioral outcomes. The current study used advanced statistical modeling to examine the impact of maternal distress during pregnancy on internalizing and externalizing problems in young children, as well as the potential mediating and moderating effects of biological, psychological, and social factors on the maternal distress-child behavior problem relationship. Methods: Women who had participated in a prospective study on maternal mood during pregnancy completed questionnaires about their child's behavior and their current mood when the child was between 1.5 and 9 years old. Maternal distress during pregnancy was constructed as a latent variable, based on a combination of self-report and clinician rated measures collected throughout the course of pregnancy. Results: Maternal distress during pregnancy was significantly associated with child behavior problems. This association was moderated by maternal social support during pregnancy. Infant baseline cortisol was also associated with child internalizing problems, but it did not act as a mediator between prenatal maternal distress and child outcome. In contrast, maternal symptoms concurrent with child behavior ratings fully mediated the maternal distress-child behavior problem relationship. Conclusions: This study extends the research on the impact of prenatal maternal distress by conceptualizing distress in a more multi-informant, comprehensive manner. The findings are discussed with regard to clinical implications and future research directions.

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Although pregnancy is often viewed as a period of great joy and excitement in our culture, there has been an increased understanding in the medical community that this time can also be a period of risk for the development or reoccurrence of a psychological or psychiatric disorder. Conservatively, it has been estimated that more than 500,000 pregnancies a year in the United States alone involve women who have a psychiatric illness that has predated or emerged during that pregnancy. There is no evidence that pregnancy decreases the risk of mental illness (Kelly, Zatzick, & Anders, 2001) or that pregnancy is a protective factor for relapse (Cohen et al., 2006).

Maternal psychological distress during pregnancy and the postpartum period has been a focus of clinical attention for thousands of years. There is evidence that as early as 400 B.C. Greek physicians such as Hippocrates were aware of the effects of emotions on pregnancy outcome (Ferreira, 1965). The past 50 years have witnessed the beginning of empirical examination of the effects of maternal psychological distress during pregnancy on the development of the child. This literature provides evidence in support of the "fetal origins hypothesis," which maintains that prenatal environmental exposures, including maternal psychological state, can alter the development of the fetus, and have lasting effects across the lifespan (Kinsella & Monk, 2009; Van den Bergh, Mulder, Mennes, & Glover, 2005).

The construct of maternal psychological distress during pregnancy has been examined and defined in the literature in a variety of different ways. For example, maternal distress has been operationalized as the presence of symptoms associated with a specific psychiatric disorder, exposure to major stressors such as natural disasters or wars, and measures of perceived stress and distress in response to daily hassles. As reviewed below, the associations noted between

these various constructs of maternal prenatal distress and behavioral outcomes of offspring are very similar.

While the majority of the literature examining the impact of maternal distress during pregnancy on child behavior problems focuses on one specific measure of distress, the current study takes advantage of multiple measures, obtained on multiple occasions during pregnancy, from more than one reporter. Specifically, maternal distress during pregnancy is constructed as a latent variable, based on a combination of self-report and clinician rated measures collected throughout the course of pregnancy. While several previous studies have attempted to examine a single construct of maternal psychological distress during pregnancy (e.g., depressive symptoms) and have relied on statistical methods to control for other types of distress (e.g, anxiety symptoms), such an approach is often problematic given the high degree of correlation among symptoms of mood disorders, stress, and distress (Goodman & Tully, 2009). In contrast, our methodological approach capitalizes on the high correlations noted between prenatal maternal distress measures by combining these measures into a latent factor that is less constrained by measure-specific error, and therefore more representative of the "true" levels of distress experienced by women during their pregnancies.

Effects of maternal psychological distress on the developing fetus

As the research on prevalence rates of mental illness and symptoms of mental illness during pregnancy has increased, a body of research examining the effects of women's prenatal psychological distress on fetal behavior has emerged. Much of this research supports the fetal origins hypothesis, which posits that prenatal environmental exposures, including maternal psychological state, can have sustained effects across the lifetime (Monk, 2001). Fetal behavior

and physiology, therefore, offer some of the first opportunities to study how maternal psychological state may have strong, and lasting, effects on the development of the child.

Fetal heart rate (FHR) and fetal activity offer non-invasive methods for examining the development of the fetuses' autonomic and central nervous system. A recent review by Kinsella and Monk (2009) found that FHR and fetal activity were associated with a wide range of maternal psychological states including perceived and laboratory induced stress, and self reported and clinically appraised depressive and anxiety symptoms. Although these findings demonstrate the immediate effects of maternal mood and distress on fetal development, they also offer insight into the lasting impact of maternal mood and distress during pregnancy. As reviewed by DiPietro, Costigan, Pressman, and Doussard-Roosevelt (2000), there is a strong continuity between fetal and infant neurobehavior, suggesting that maternal distress during pregnancy not only influences the neurodevelopment of the fetus, but also outcomes during infancy and later childhood. Measures of fetal heart rate variability have been shown to be significantly associated with mental and psychomotor development during early childhood (DiPietro, Bornstein, Hahn, Costigan, & Achy-Brou, 2007), illustrating how prenatal physiological states may reflect a neurodevelopmental process that unfolds throughout childhood.

Fetal programming hypothesis

The fetal programming hypothesis is derived from human epidemiological and animal model data and suggests "when disturbing factors act during specific sensitive periods of development, they exercise organizational effects – or program some set points" (Van den Bergh & Marcoen, 2004, p. 1087). This can have lifelong effects on the organism because the programmed set points do not readapt if the environment changes later in life, which then creates

a “mismatch” between capacities set early in life and the future environments that the organism must later function in. For example, a fetus whose ability to metabolize glucose was set during a period of famine is often unable to adjust to a dramatic improvement in nutritional environment that occurs after birth, increasing the likelihood that he or she will develop childhood diabetes (Barker, 1998). In animals, the hypothalamic-pituitary-adrencortical (HPA) axis is extremely susceptible to perinatal programming by glucocorticoids. Multiple studies have shown that prenatally stressed animals show lifelong abnormalities in their endocrinologic stress response, as well as behavioral symptoms related to the dysregulation of the HPA axis including fearfulness, anxiety, and maladaptive coping to new situations (Van den Bergh & Marcoen, 2004).

In recent years, the fetal programming hypothesis has been put forth as a way of explaining the impact of early childhood experiences on later psychological development (O’Connor, Heron, Golding, & Glover, 2003; Van den Bergh & Marcoen, 2004). The evidence from the animal literature that prenatal stress/anxiety occurring at discrete periods during pregnancy is associated with a range of later behavioral and neurological disturbances, along with the human literature connecting prenatal stress/anxiety with poor obstetric outcomes, have formed a solid base of evidence for fetal programming. Studies linking prenatal mood disturbances to behavioral outcomes in children remain the next step in validating this hypothesis.

Potential pathways of transmission

Although the pathway between maternal prenatal mood and fetal development has not yet been fully characterized, the endocrine system is a likely method of transmission of maternal mood to the fetus (Sandman, Glynn, Wadhwa, Chicz-DeMet, Porto, & Garite, 2003; Teixeira,

Fisk, & Glover, 1999; Wadhwa et al., 2002). In the first step of this process anxiety and stress during pregnancy activate the mother's HPA axis, resulting in the release of cortisol. Maternal cortisol is not fully metabolized by the placenta; therefore, an increase in maternal cortisol likely results in fetal glucocorticoid exposure (O'Connor, Ben-Shlomo, Heron, Golding, Adams, & Glover, 2005). This has been demonstrated by multiple studies that have shown significant correlations between maternal pituitary-adrenal stress hormones such as ACTH and cortisol and placental CRH levels (Wadhwa, Sandman, Chicz-DeMet, & Porto, 1997). Significant correlations between maternal and fetal plasma cortisol levels have been found (Gitau, Fisk, Teixeira, Cameron, & Glover, 2001), suggesting a possible pathway of maternal to fetal risk. Our lab has recently shown that neonatal and maternal HPA axis activity at delivery are highly coupled, with positive associations between maternal and neonatal plasma levels of ACTH, total cortisol, and free cortisol (Smith, et al., in press). Animal models have shown that the fetal HPA axis is especially vulnerable, and that given this sensitivity, the HPA axis may be "programmed" by maternal distress (O'Connor et al., 2005). The findings from animal models and studies linking maternal mental illness to changes in the physiological functioning of the fetus lay the groundwork for understanding how maternal psychological state during pregnancy can impact the later behavior of the child. As reviewed below, the current study will test this potential method of transmission as a mediator of the association between maternal psychological distress during pregnancy and childhood outcomes.

Maternal Psychological Distress During Pregnancy and Child Behavior Outcomes

As previously discussed, the majority of studies that examine the impact of maternal distress during pregnancy on child behavior focus on only one aspect of distress, while either ignoring or statistically controlling for other types of distress. Prenatal maternal symptoms of

depression, anxiety, or stress are the most common types of distress studied and are most often assessed using self-report measures such as the Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1997), the Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1987) (depression), the Speilberger State-Trait Anxiety Inventory - State (STAI-S; Speilberger, 1983) (anxiety), and the Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983) (stress). Child behavior is most often assessed by parental report on a standardized questionnaire, most commonly the Child Behavior Checklist (CBCL; Achenbach, 1991). The CBCL provides a total behavior score (with a high score indicating more problem behaviors) as well as subscale scores on internalizing and externalizing disorder symptoms.

Because of the current nature of the literature, the studies examining the impact of maternal distress during pregnancy on child behavior are categorized and reviewed below based on primary definition of distress as defined by the author. Other measures of distress included in each study are noted, as well as any observed gender differences.

Depression symptoms. In a relatively small study examining the relationship between depressive symptoms during pregnancy and a range of developmental outcomes, Carter, Garrity-Rokous, Chazan-Cohen, Little, and Briggs-Gowan (2001) found that maternal depressive symptoms during pregnancy were significantly associated with externalizing problems as measured by the CBCL in boys at age two and a half. No significant associations between maternal depressive symptoms and behavior problems were found for the girls. This study did not examine any other constructs of maternal distress. Of note, while the sample used in this study was not described as clinical, over 50% of the sample had a lifetime history of depression or depression and at least one other comorbid psychological condition. Although the authors concluded that perhaps prenatal depressive symptoms differentially affect boys and girls, the

small sample size and limited assessments of the mothers during pregnancy suggest that this conclusion may be premature. However, despite the methodological limitations of the study, direct associations between maternal depressive symptoms during pregnancy and preschool child behavior problems were noted.

Associations between mother's prenatal depressive symptoms and child behavior were also found in a separate sample of school-aged children (Luoma et al., 2001). This author reported that children whose mothers experienced prenatal depressive symptoms scored higher on the CBCL Externalizing and Total Problems scales than children of nonsymptomatic mothers. A similar trend was also seen when teacher reports of the CBCL were examined, although the results did not reach statistical significance. In logistic regression analyses, high levels of maternal prenatal depressive symptoms predicted higher scores on child Externalizing Problems and Total Problems scales (a combination of maternal and teacher report) even after accounting for maternal postpartum depressive symptoms measured at two months. In this study, gender did not demonstrate a significant moderating effect.

The results from these initial studies indicate that depressive symptoms during pregnancy may significantly impact child behavior, specifically increasing the amount of externalizing problems displayed by the child. While there is some preliminary evidence for specific gender effects, this remains a largely unexplored question.

Anxiety Symptoms. Many of the existing studies linking maternal anxiety symptoms during pregnancy and child behavior problems come from the ALSPAC team, as this is the largest prospective cohort currently being followed to examine the associations between symptoms of stress, anxiety, and depression during pregnancy and child outcome. Other investigators such as Van den Bergh (2004; 2006) have studied a similar, but older cohort,

focused on outcomes during middle childhood and adolescence. Each of these investigators used a similar study design with regards to the utilization of statistical methods to control for prenatal and postpartum depression and postpartum anxiety.

The investigators from the ALSPAC team first reported a link between stress and anxiety symptoms during pregnancy and behavioral and emotional problems in young children in 2002 (O'Connor, Heron, Golding, Beveridge, & Glover, 2002). This study focused on prenatal symptoms of anxiety and parent reports of child behavior at 47 months (3.9 years). The results from this study were notable. The mothers who scored in the top 15% of the sample on the anxiety measure (assessing anxiety symptoms) at either 18 or 32 weeks gestation were 2-3 times more likely to have a child who scored more than two standard deviations above the mean on measures of inattention/hyperactivity, emotional problems, and conduct problems. When antenatal, obstetric, and psychosocial covariates, as well as postnatal anxiety and depressive symptoms were controlled for, these findings remained significant for the composite measure of total problems of boys and girls for mothers with high anxiety at 32 weeks gestation. In this model, early prenatal anxiety, postnatal (8 weeks) anxiety, and postnatal depression had almost no effect on the magnitude of the prenatal prediction. The only gender difference noted in this study was that late prenatal anxiety was also significantly associated with hyperactivity/inattention for boys, after controlling for the prenatal, obstetric, and psychosocial covariates mentioned above (O'Connor et al., 2002).

The next study from the ALSPAC team examined the behavior/emotional problems in the children when they were approximately six years old (O'Connor, Heron, Golding, & Glover, 2003). Based on the findings from the previous study that late prenatal anxiety had the greatest effect on child behavior, this paper focused exclusively on this time period. This study showed

that a high number of maternal anxiety symptoms during pregnancy were associated with increased risk for total behavior problems, hyperactivity, emotional problems, and conduct problems in both boys and girls. These findings remained significant even after controlling for antenatal, obstetric, and psychosocial confounds such as birth weight, gestational age, and postnatal symptoms of anxiety and depression. When postnatal assessments of anxiety and depression were added to the model, prenatal anxiety remained a strong and significant predictor for all subscales, but associations between postnatal anxiety and emotional problems in boys, postnatal anxiety and conduct problems in girls, and postnatal depression and conduct problems in boys were also noted.

Similar to the ALSPAC study, Van den Berg and colleagues also investigated the associations between anxiety symptoms during pregnancy and child behavior outcomes. In one study (Van den Bergh & Marcoen, 2004) they examined reports of the child's behavior at age eight years from several sources – the mother, a teacher, an external observer during a home visit, and the child. From these reports, four composite scores were constructed: ADHD symptoms, externalizing problems, internalizing problems, and self-reported anxiety. Similar to the studies described above, potential confounding variables were controlled for, including the child's gender, birth weight, and maternal postnatal trait anxiety. Of note, prenatal and postnatal maternal depression where not examined in these analyses. After other variables were controlled for, symptoms of prenatal anxiety were significantly associated with ADHD symptoms, externalizing problems, and self-reported anxiety in the children, explaining between 9 and 22% of the variance.

Van den Berg and colleagues also used an objective, computerized task to examine ADHD symptoms in adolescents in association with maternal symptoms of prenatal anxiety (Van

den Bergh et al., 2006). The continuous performance task (CPT) is a measure of sustained attention and self-regulation and is often used clinically in the diagnosis of ADHD. The CPT requires the resistance of potentially distracting stimuli, and therefore can be a very difficult task for children and adolescents with ADHD. This study found that boys of mothers who had reported a high number of anxiety symptoms during early pregnancy (12-22nd week) showed a decline in performance during the task such that their processing speed became slower and there was more variability in their reaction times. These findings remained significant after controlling for intelligence as well as postnatal maternal trait anxiety and parental intelligence level. Of note, these findings did not extend to the girls in this sample, where no significant associations between prenatal anxiety symptoms and child attentional problems were found.

Stress. Perceived levels of stress during pregnancy are highly comorbid with symptoms of depression and anxiety (Molfese, Bricker, Manion, & Beadnell, 1987). However, many researchers have examined the effects of stress independently of symptoms of anxiety and depression. Higher levels of maternal perceived stress during pregnancy were found to be associated with more total problems and more externalizing problems on the CBCL in toddlers. These behaviors included easy frustration, more angry moods, and more crying (Gutteling et al., 2005). As mentioned by the authors, these findings are similar to those of O'Connor et al., who found increased levels of conduct problems and emotional problems in four year olds who had been exposed to high levels of prenatal anxiety (2002).

Perceived stress during the prenatal period has also been linked to parent and teacher reports of ADHD symptoms in school-age children. Rodriguez and Bohlin (2005) examined whether smoking and/or stress during pregnancy were associated with ADHD diagnostic criteria in children at age seven. Although only a small percentage of the sample met diagnostic criteria

for ADHD (about 4%) and all were male, the investigators found stress during pregnancy predicted ADHD symptoms independently of smoking. The strongest effects were found when the stress occurred at the beginning of the pregnancy (10 weeks gestation).

As described in this section, maternal depressive symptoms, anxiety, and stress during pregnancy have each been linked to behavior problems in toddlers, children, and adolescents. The findings from studies examining these three sets of maternal symptoms show significant overlap, and this is likely due to the high correlation between maternal symptoms of depression, anxiety, and stress. This overlap supports the suggestion by Moffit, Harrington, Caspi, Kim-Cohen, Goldberg, Gregory, and Poulton (2007), and the view taken by the author, that these types of measures should be combined into a single construct of prenatal maternal distress in the study of associations with child outcomes.

Mediators and moderators of the relationship between maternal prenatal distress and child behavior

While examining the associations between prenatal maternal psychological distress and child behavior was the first aim of this paper, understanding how biological, psychological, and social factors might mediate and moderate this relationship was also of great interest. The infant's HPA axis functioning, heritability, course of maternal symptoms during pregnancy, and social support during pregnancy are all relevant to child developmental outcomes. The current project adds to the existing literature by testing whether the infant's HPA axis functioning at six months mediates the relationship and if heritability, course of symptoms, and social support moderate the relationship between maternal prenatal psychological distress and child outcomes. Theoretical rationales are discussed within the context of fetal programming and the biopsychosocial model of risk.

Infant HPA axis functioning. The hypothalamic-adrenal-pituitary (HPA) axis controls the body's reaction to stress and is normally activated during a physical or emotional stressor. However, altered functioning of the HPA axis is strongly associated with adult major depressive disorder (MDD); in fact, this association has been referred to as one of the most consistent findings in biological psychiatry (Paroamte & Miller, 2001). Alterations in the HPA axis have also been noted in individuals with anxiety disorders, most regularly in PTSD (Yehuda, 2009). While alterations in the HPA axis were initially believed to be related to symptomology, animal studies and clinical findings in humans have lead the field to a much more complex model that includes preexisting differences in the HPA axis due to genetic risk factors and early adverse life events, making certain individuals more vulnerable to the development of a psychiatric disorder later in life. This idea is supported in both the depression literature (e.g. Holsboer, 2000) and the PTSD literature (e.g. Yehuda, 2009).

As discussed previously, there is mounting evidence that maternal mood during pregnancy is related to lasting changes in the physiological functioning of the fetus through the impact of the maternal endocrine system. Elevated maternal cortisol levels have been associated with fetal activity and behavior, including failure to show habituation to stimuli (Sandman et al. 1999) and an attenuated startle response (Rothmensch, Celentano, Liberati, Sadan, & Glezerman, 1999). Field and colleagues have demonstrated that fetal activity and weight are associated with maternal urinary cortisol levels between 20 and 28 weeks gestation (Field & Diego, 2008). Maternal HPA axis activity during pregnancy is also directly related to neonatal cortisol levels. Infants of women who were depressed during their third trimester of pregnancy (and had accompanying higher levels of cortisol) showed the same pattern of elevated cortisol as their mothers (Lundy et al., 1999). Altered HPA axis activity in both the mother and the neonate has

been hypothesized to directly impact newborn behavior. High infant cortisol has been linked to difficulty with newborn behavior regulation (as measured by the Brazelton Neonatal Behavior Assessment Scale) and higher levels of irritability (Field & Diego, 2008; Graham, Heim, Goodman, Miller, & Nemeroff, 1999). Longitudinal studies have noted that maternal mood during pregnancy is associated with individual differences in awakening and afternoon cortisol levels in ten-year-olds. (O'Connor et al., 2005). Taken together, these findings suggest the potential mediating role of cortisol in the relationship between maternal prenatal distress and infant behavior.

Genetic Influences. It has been well established that children of parents with mental illness have a substantially increased risk for developing a variety of psychopathological disorders. During the last ten years, the understanding of the genetic contribution to the development of mental disorders has grown, and specific candidate genes are now being identified as potential routes of transmission. The strength of the genetic contribution to the development of mental disorders is estimated from examining the incrementally higher concordance in mental disorders between relatives who share larger proportions of their genomes (Uher, 2009). Twin and adoption studies are used to partition the effects of genetics from environment. Heritability can, therefore, be defined as the estimated contribution of additive genetic effects. In a recent review, Uher examined heritability estimates for psychiatric disorders. Relevant to the current study, the heritability estimate for MDD is .37, and for anxiety disorders is .32 (Uher, 2009).

Many investigators have looked to the serotonin system to understand how genetic risk for the development of psychopathology is transferred from parent to child. The serotonin system has been examined as a logical source of candidate genes for mood disorders, since

serotonin function plays a role in modulating mood states, and has been implicated in mood and anxiety disorders (Hariri & Holmes, 2006). One of the first papers to report the link between the serotonin system and mood disorders was authored by Caspi and colleagues (2003), who showed that while there was no main effect of the serotonin transporter long polymorphic region (5HTTLPR) genotype on depressive symptoms, there was a significant interaction between the occurrence of stressful life events, and genotype (i.e., the presence of an S-allele) in predicting the magnitude of depressive symptoms experienced by the individual. For participants who had either the SS or SL genotype, stressful life events predicted the onset of new and recurrent episodes of depression (Caspi et al., 2003). The strength of these findings is currently under debate. While Caspi and others have replicated this finding, a recent meta-analysis of published and unpublished data by Risch and colleagues (2009) yielded no evidence that the serotonin transporter geneotype was associated elevated risk for depression, nor that the genotype interacted with stressful life events to increase the risk of depression.

The impact of genetic risk has begun to be examined in the context of the fetal programming hypothesis, in that the impact of maternal distress during pregnancy on infant outcome may vary across fetuses due to their genetic make-up. Pluess and colleagues investigated how the association between self-reported maternal anxiety midway through pregnancy (20 weeks) and mother-rated infant negative emotionality at 6 months was impacted by the child's genotype (In press). They found that infants with the 5-HTTLPR short allele were rated as having more negative emotions when their mothers reported prenatal anxiety. Interestingly, there was no association between genotypes and infant negative emotionality in cases where mothers reported low anxiety during pregnancy, suggesting a significant gene by environment interaction.

The current study will examine the moderating effect of 5-HTTLPR genotypes on the relationship between maternal psychological distress during pregnancy and child behavior. It is hypothesized that the risk (short) allele will increase the vulnerability of the child to stressful prenatal environments, and therefore the likelihood for the child to develop behavior problems.

Timing of maternal symptoms. The impact of the timing of maternal distress is central to the fetal programming hypothesis. Given that fetuses develop at such a rapid pace and that different physiological systems develop at different points in pregnancy, researchers have questioned whether consequences of exposures during fetal development may vary depending on the timing of that exposure in pregnancy. More specifically, it has been posited that at each stage of gestation, different areas of the fetal brain are developing rapidly, and an area of the brain under rapid development may be more vulnerable to the effects of maternal psychological distress.

While there is agreement that the timing of the event during pregnancy potentially matters when examining developmental outcomes, methodological limitations in the existing literature do not allow for conclusive evidence in this regard. Many studies (Carter et al., 2001; Luoma et al., 2001) measure symptoms of maternal psychological distress only once during pregnancy, and therefore do not allow for comparisons of groups exposed during a specific period. While other studies measure maternal symptoms throughout pregnancy (Gutteling et al., 2005; Rodriguez & Bohlin, 2005), they average all ratings together, providing only a "mean" measure of exposure, which makes it difficult to assess the effect of gestational timing.

The studies from the two most well-established datasets on maternal psychological distress in pregnancy (O'Connor et al., 2002; O'Connor et al., 2003; Van den Bergh & Marcoen, 2004; Van den Bergh et al., 2006) measured and reported symptoms at two or three discrete

periods during pregnancy, making examination of the timing of the symptoms possible. Interestingly, while the ALSPAC team and Van den Bergh both examined measures of anxiety during early (12-22 weeks) and late (32-40 weeks) pregnancy, their findings significantly differed with regards to timing. O'Connor and colleagues (2002; 2003) found that exposure to maternal anxiety during late pregnancy was significantly related to child behavior problems, while Van den Bergh (2004; 2006) found that exposure to maternal anxiety during early pregnancy was the strongest predictor of future behavior problems. It should be noted that the children in O'Connor's studies were significantly younger than those in Van den Bergh's, so this is a possible explanation for the discrepancies in the findings. However, this highlights the gaps in knowledge that exist with regards to the timing of maternal prenatal psychological distress and how this factor may influence child outcome.

In the current study we measured maternal psychological symptoms at multiple times during pregnancy. Timing was examined by comparing the impact of maternal distress during each trimester on child behavioral outcomes. Because of the inconsistencies in the literature, this hypothesis was exploratory in regards to direction of association.

Social support. Pregnancy constitutes a time of significant life change for women and their partners. Major sources of stress include changing roles and relationship difficulties. As reviewed by Glazier, Elgar, Goel, and Holzapfel (2004), studies have shown that partner conflict during pregnancy is related to emotional distress, pregnancy worries, and inversely related to perceived social support. Marital, family, and social support play a large role in most theoretical models of MDD and other mental illnesses, whether as an etiological factor, a consequence, or as sharing common causes (Joiner, 2002). MDD commonly co-occurs with perceptions of relationships being less supportive or available (Brown & Harris, 1978; Fredman, Weissman,

Leaf, & Bruce, 1988) and with disruptions in marital relationships and psychopathology in partners (Beach & Nelson, 1990). In community samples of pregnant women, there has been support for the association between depressive symptoms and lower social support as well as poorer marital adjustment (O'Connor, Hawkins, Dunn, Thorpe, & Golding, 1998; Zelkowitz, Schinazi, Katofsky, Saucier, Valenzuela, & Westreich, 2004). While these studies examine the relationship between depressive symptoms and marital support, very few studies have looked at how support could influence the association between maternal psychological distress and pregnancy (or child behavioral) outcomes. One study found social support interacted with life stress to predict pregnancy complications (Norbeck & Tilden, 1983), while another noted that social support during pregnancy mediated the effects of maternal negative emotionality on infant cardiac vagal tone (Ponirakis, Susman, & Stifter, 1998).

In the current study we examined social support throughout pregnancy using the Dyadic Adjustment Scale (DAS). The DAS assesses the quality of the marital or partner relationship and gave us a quantitative measure of how the participant viewed her relationship with her partner (with higher scores indicated a more positive view). The current study extends the findings in the existing literature by examining how relationship satisfaction moderates the relationship between prenatal psychological distress and child behavior. It was hypothesized that higher levels of relationship satisfaction would lessen the impact of maternal prenatal psychological distress on child behavioral outcomes.

Potential Confounds

As reviewed below, medication exposure during pregnancy and the association of child behavior problems with postpartum or current depressive symptoms have been identified in the literature as potential confounds when examining the relationship between maternal

psychological distress during pregnancy and child behavior problems. Gender of the child has also been found to be important when examining the association between maternal psychological distress and child behavior problems in some (e.g., Van den Bergh et al., 2006) but not all (e.g., O'Connor et al., 2002) studies. In the current study both medication exposure during pregnancy and child gender were examined as potential covariates. Maternal depressive symptoms at follow-up were also examined in an exploratory fashion as a mediator between maternal prenatal distress and child behavior outcomes.

Medication exposure. Medication is currently the most widely used treatment for mood and anxiety disorders and prescription of psychotropic medication during pregnancy has been increasing steadily over the past decade. Clinical research has shown that all classes of psychotropic medications readily cross the placenta and enter into fetal circulation, and that fetal exposure may be comparable to the plasma concentrations associated with direct treatment (Newport et al., 2007). Prospective studies that examine the effects of prenatal psychotropic medication on the child have been inconsistent, with some studies finding no effect (Nulman, Laslo, Fried, Ulerkyk, Lishner, & Koren, 1997), and others showing that some infants exposed prenatally demonstrate neuromotor symptoms following delivery (Sanz, De-las-Cuevas, Kiuru, Bate, & Edwards, 2005). Our lab recently found that prenatal exposure to psychotropic treatment seemed to offset the effects of prenatal maternal symptoms of anxiety and depression on infant cortisol levels, suggesting lasting but ameliorative effects (Brennan, Paragas, Walker, Green, Newport, & Stowe, 2008). Because there is no doubt that the effects of prenatal medication on child behavior are important and potentially significant, this study will examine medication exposure as a potential confound, and statistically control for it if necessary.

Maternal depressive symptoms at follow-up. Depression, stress, and anxiety are often chronic in nature, making it important to examine how concurrent maternal symptoms impact the association between maternal distress during pregnancy and child behavioral outcomes. There is no standard in the field about how best to examine the potential impact of current maternal symptoms on the association between maternal distress during pregnancy and child behavioral outcomes. Some studies simply do not examine the impact of current maternal symptoms (e.g. Rodriguez & Bohlin, 2005) while others use statistical methods to control for current maternal symptoms (e.g., O'Connor et al., 2002; O'Connor et al., 2003, Van den Bergh & Marcoen, 2004). Given the chronic nature of symptoms of depression, stress, and anxiety, and therefore the likelihood that distress during pregnancy will be highly correlated with current maternal symptoms, the current study examined current maternal symptoms as a potential mediator of the relationship between maternal distress during pregnancy and child behavioral outcomes.

Rationale for the Current Study

While many studies have demonstrated associations between maternal psychological distress and negative child outcomes, exposure to maternal distress during the prenatal period is often overlooked. Furthermore, while individual studies have examined how maternal symptoms of prenatal depression, anxiety, or stress are related to child behavior, the overlapping and combined effects of these distress measures have not been evaluated. Additionally, many of the factors that theoretically may mediate or moderate the relationship between maternal psychological distress and child behavior have not been examined during the prenatal period. This study attempted to fill these existing gaps in the literature by examining the association between prenatal maternal psychological distress and child behavior problems, and by testing

several potential mediators and moderators of this association. The specific hypotheses of this study were:

1. Maternal psychological distress during pregnancy will be positively associated with child behavioral problems.
2. The child's cortisol levels at six months will mediate the association between maternal psychological distress during pregnancy and child behavioral problems.
3. The association between maternal psychological distress during pregnancy and child behavioral problems will be stronger in the presence of an S-allele on the serotonin transporter gene-linked polymorphism region in the child.
4. The association between maternal psychological distress and child behavioral problems will be stronger in women with low levels of relationship satisfaction during pregnancy.

Because of the inconsistencies and gaps in the literature, three additional hypothesis were exploratory in nature:

5. The timing of the exposure to maternal psychological distress will moderate the association between maternal psychological distress during pregnancy and child behavioral problems.
6. The gender of the child will moderate the association between maternal psychological distress during pregnancy and child behavioral problems.
7. Current maternal depressive symptoms will mediate the association between maternal psychological distress during pregnancy and child behavioral problems.

Method

Overview

Participants were drawn from a cohort of women and children who had been assessed by the Emory Women's Mental Health Program (WMHP) in the Department of Psychiatry at the Emory University School of Medicine. The WMHP is a referral center for the treatment of mental disorders during pregnancy and the postpartum period. As delineated below, maternal psychological distress was evaluated at set time points throughout pregnancy using a variety of measures. The current and past studies were approved by the Human Subjects Institutional Review Board at Emory University and all women who participated provided written informed consent.

Inclusion/Exclusion Criteria

Maternal Inclusion Criteria:

1. Completed pregnancy protocol for a WMHP study.
2. Child of the completed pregnancy protocol was aged 1.5-9 years old.
3. Lifetime history of a mood or anxiety disorder.
4. Written and verbal fluency in English.
5. Ability to give informed consent and comply with study procedures.

Maternal Exclusion Criterion:

1. Primary diagnosis of bipolar disorder, schizophrenia, and/or currently active eating disorder.

Participants

The sample consisted of 162 women and their children (83 boys and 79 girls). The demographic composition of the sample was approximately 95% White, .5% African American, 1.5 % Asian, and 3% representing other racial/ethnic groups. 82% of participants had a primary lifetime diagnosis of a mood disorder, 17% of participants had a primary lifetime diagnosis of an

anxiety disorder, and .6% of participants had a primary lifetime diagnosis of a somatoform disorder (with a secondary diagnosis of an anxiety disorder).

Recruitment was conducted by contacting eligible participants and offering them the opportunity to participate in the child follow-up study. Contact was first made by mail, and then by phone. Three hundred and thirty two women were invited to participate in the follow-up study. One hundred and sixty two completed the follow-up measures (49%). As shown in Table 1, the women who participated in the follow-up study were more likely to have planned the target pregnancy (69% vs 51%) and had slightly more years of education (16.7 years vs 16.0 years). There were no differences in maternal age at delivery, race, marital status, gender of the baby, or postnatal complications. On the clinical measures during pregnancy, the women who participated in the follow-up study had lower scores on the BDI and PSS. No significant differences were noted on baseline diagnoses, the CGI, the HRSD or relationship satisfaction. Given the higher levels of symptoms during pregnancy in the women who chose not to participate in the current study, the findings are likely an underestimate of the impact of maternal distress on child behavioral outcomes.

Procedures

Psychosocial assessment during pregnancy. At the WMHP there is an established protocol for psychosocial assessment during pregnancy that spans all research studies conducted in the program. At study entry, current and lifetime diagnostic information was assessed using the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995) and a primary lifetime diagnosis was assigned. At the baseline and all subsequent follow-up visits (occurring at 12, 16, 20, 24, 30, 32, and 36 weeks gestation), participants met with a study psychiatrist, who assigned a Clinical Global Index (CGI) score for each week of pregnancy, and a research assistant, who

administered the 17-item Hamilton Rating Scale for Depression (HRSD 17). Self-report measures were completed which included measures of stress (Perceived Stress Scale, PSS), depression (BDI), and social support (DAS). A subsample of the clinical interviews are double-coded on an ongoing basis to ensure adequate inter-rater reliability.

DNA collection. At the last pregnancy visit (approximately 36 weeks gestation), participants were given information about umbilical cord blood samples as well as a collection kit with instructions for the obstetrician and/or midwife. Umbilical cord blood samples were obtained following each birth and placed immediately on slush ice until retrieved by WMHP staff. Plasma was separated by centrifugation at 2C within 30-60 minutes and were frozen on dry ice and stored at -80C until analyzed. Samples were successfully collected from 82 children. There were no differences between the subsample of participants with DNA data and those without on measures of maternal symptomatology during pregnancy or child behavior problems.

HPA axis collection. For a subsample of the children (n = 86) salivary cortisol data were available from infancy. These data were collected during a laboratory visit when the infants were six months old. All laboratory visits began at 1:00 pm to control for the diurnal rhythm of cortisol. Infant salivary cortisol measures were obtained at baseline and in reactivity to a laboratory stressor task. Full study procedures can be found in Brand et al., (2010). There were no differences between the subsample of participants with cortisol data and those without on measures of maternal symptomatology during pregnancy or child behavior problems.

Operational Definitions

Maternal psychological distress. Based on the literature reviewed above, it is clear that maternal distress during pregnancy is related to child behavior. However, no single study has taken symptoms of maternal distress such as depression, stress, and psychiatric functioning,

which often are highly correlated, and constructed a single measure of psychological distress. In the current study, Structural Equation Modeling (SEM) was used to construct a latent variable of maternal psychological distress, taking advantage of multiple measures of distress (depression, psychiatric functioning, and stress) from a variety of sources (clinician, objective, and subjective). This technique allows for a much more accurate profile of distress during pregnancy and also minimizes the error associated with single measures.

The construct of maternal psychological distress also takes advantage of the multiple data collection points during pregnancy. 'Area under the curve' (AUC) indices for each symptom measure across gestation and across the first, second, and third trimesters, were calculated to provide indices of cumulative exposure. By convention, the first visit was carried back to conception and the last measure forward to delivery to provide the AUC. While it is acknowledged that this will not be the best measure for very early pregnancy and from the final visit to delivery, this remains the best option for capturing the longitudinal nature of the data across pregnancy to the fullest extent.

Child behavior. In the current study, child behavior was assessed when the child was between 1.5 and 9 years of age. The CBCL (as reviewed below) assesses child behavior across many domains including affective problems, anxiety problems, somatic problems, ADHD problems, oppositional defiant problems, and conduct problems. Two subscale scores, Internalizing Problems and Externalizing Problems were used as the primary measures of child behavior problems in this study.

Maternal Symptom Measure – Clinician Rated

Clinical Global Index (CGI) (Guy 1976). The CGI was assigned by the study psychiatrist based on a clinical interview reflecting psychiatric symptom status for each week of pregnancy.

The CGI provides a global rating of the severity of the participant's disorder or symptoms, and thus provides a cross diagnosis assessment of the severity of the symptoms.

Maternal Symptom Measures – Research Assistant Rated

Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition (SCID) (First, Spitzer, Gibbon, & Williams, 2002). The SCID is a structured clinical interview administered by a trained research assistant that assesses for lifetime history and current presence of an Axis I disorder. The interviewer asks structured questions to determine the presence or absence of symptoms of each disorder. In research studies the SCID has been shown to be a valid and reliable measure of anxiety and mood disorders (kappas ranging from .70-.80) (Zanarini & Frankenburg, 2001). The SCID is often considered the "gold standard" for the assessment of Axis I pathology (Shear et al., 2000). In the current study, the SCID was used to establish the presence of a lifetime disorder for inclusion into the study. Interrater reliability for the current study was well established with kappas for each disorder exceeding 0.8.

Hamilton Rating Scale for Depression (HRSD) (Hamilton 1960). The HRSD is a 17-item scale that is completed by a trained research assistant in the context of a semi-structured interview to assess symptoms of depression. The interviewer provides ratings on items including overall level of depression, guilt, feelings of worthlessness, suicide, insomnia, and physical symptoms within the last week. Thirteen of the items are scored on a five-point scale with a score of 0 = complete absence of the symptom, 2= mild symptom, and 4=severe symptom. Three items are scored on a four-point scale with a score of 0 = complete absence of the symptom and 3= presence of a severe symptom. The remaining ten items are scored on a three point scale, with 0=absence of the symptom and 2= clear presence of the symptom. Scores on this scale range

from 0-81, with higher scores indicating more severe symptoms of depression. This scale has been shown to be a reliable and valid measure of depressive symptoms (Williams 1989).

Maternal Symptom Measures – Self Report

Perceived Stress Scale (*PSS*) (Cohen, Kamarck, & Mermelstein, 1983). The Perceived Stress Scale is a 14-item self-report questionnaire that measures an individual's evaluation of the stressfulness of the situations in their lives over the past month. Questions ask about thoughts and feelings around situations such as something happening unexpectedly, ability to handle personal problems, and events occurring outside of 'your' control. For each question, scores range from 0 = never to 4 = very often. The PSS has been shown to have good reliability and validity across samples (Cohen, et al., 1983).

Beck Depression Inventory (BDI) (Beck, Steer, & Brown, 1997). The BDI is a 21-item self-report scale assessing the intensity of depressive symptoms in the previous two weeks, with higher scores revealing more severe levels of depression symptoms. The symptoms listed and the time-frame addressed are consistent with the DSM-IV. Scores greater than 13 indicate at least mild depression. The BDI has high internal consistency, good test-retest reliability, and good construct, concurrent, and discriminate validity in clinical and nonclinical samples (Steer, Ball, Ranieri, & Beck, 1997; Whisman, Perez, & Ramel, 2000).

Mediator Measures

HPA Axis Assay. Four infant saliva samples were collected in the context of a separate laboratory study on stress sensitivity in infancy. Saliva samples were frozen at –20 °C within 15 minutes of collection. Saliva was assayed for cortisol concentration using a commercially available radioimmunoassay kit (DiaSorin GammaCoat, Stillwater, Minnesota). Sensitivity for saliva cortisol is 0.05 mcg/dL, and inter- and intra-assay coefficients of variation are 6.0% and

3.5% respectively. Infant saliva measures were assessed along two dimensions for the current study: 1) baseline (study entry) and 2) HPA axis reactivity calculated as the area under the curve (linear trapezoid method) for three post-stressor saliva samples of cortisol, as measured from baseline. Cortisol measures were log transformed prior to data analysis.

Maternal Depressive Symptoms at Follow-up: The BDI (described above) was completed by the mother at the same time as the CBCL.

Moderator Measures – Self Report

Dyadic Adjustment Scale (*DAS*) (Spanier, 1976). The DAS is a self-report measure of relationship adjustment. The DAS assess the degree of satisfaction or dissatisfaction couples are experiencing. Lower scores indicate for dissatisfaction in relationships. The DAS has demonstrated good content, criterion-related, and construct validity.

Moderator Measures – Biological Assays

DNA extraction and 5HTTLPR genotyping. DNA was extracted from whole blood using the Qiagen M48 biorobot (Qiagen Inc). Genotyping of the 5-HTTLPR used the following primers (forward: 5'-Hex-TGAATGCCAGCACCTAACC -3'; reverse: 5′-ATACTGCGAGGGGTGCAG -3′). PCR was carried out in 384 well plates in a 10 µl volume with 10 ng DNA. Each PCR reaction contained 0.5 µM of each primer, 0.08 µM of dATP, dCTP and dTTP and 0.04 uM of dGTP, 0.2 µM of 7-deaza GTP (Amersham Biosciences), 5% DMSO and 1.25 units of AmpliTaq Gold (Applied Biosystems). The cycling parameters were as follows: 95˚C for 5 min, then 94˚C for 30sec, 63˚C for 30 sec and 72˚C for 1 min for 1 cycle, then the annealing temperature was reduced to 62˚C for one more cycle and then to 59.5˚C for 38 cycles. 5 µl of the resulting PCR products was then digested with 5 U MspI (New England Biolabs) in a total volume of 10 µl for 90 minutes at 37°C to detect the A/G SNP rs25531 shown

to influence the functional effects of the long and short alleles. The digested PCR products were then separated using an Applied Biosystems 3100 genetic analyzer and analyzed with Applied Biosystems Genemapper 4.0 software. Fragment lengths for the L_A-allele are 291 bp, 148 for the L_G and 247 bp for the S-allele. The VL fragment is 335 bp and the XL fragment 375 bp. The L-VL or L-XL genotypes were each observed in one participant; both were excluded from the analysis. For quality control, the runs included duplicated samples and positive controls established through re-sequencing.

Child Behavior Measure – Mother Rated

Child Behavior Checklist (CBCL) (Achenbach, 1991). Child behavior problems were assessed by maternal report on the CBCL, one of the most well validated measures of child behavioral functioning (Achenbach & Edelbrock, 1983; Achenbach & Rescorla, 2001). The CBCL has been used to identify children at high risk for future psychopathology within a population of children already at risk by virtue of parental psychopathology (Petty et al., 2008). The CBCL early years was given to children between the ages of 1.5-5, and the CBCL school years was given to children between the ages of 6-9. Mothers were asked to describe behaviors of their child that occur now or within the past 30 days. For the CBCL (early years and school years) higher scores indicate greater problem behaviors.

The CBCL early years obtains maternal ratings on 99 problem items plus descriptions of problems, disabilities, and concerns about the child. Responses to items are 0 (not true), 1 (sometimes true), and 2 (very true or often true). Symptoms of Internalizing Problems (e.g. depression and somatic complaints), Externalizing Problems (e.g., emotional reactivity and aggressive behaviors), and Other Problems (e.g., sleep and attention) are combined into an overall Total Problem score.

The CBCL School Years consists of 113 behavior problem items. Responses to items are 0 (not true), 1 (sometimes true), and 2 (very true or often true). Broadly, these rating scales tap symptoms of Internalizing Problems (e.g., depression and anxiety), Externalizing Problems (e.g., aggression, conduct problems, attention-deficit/hyperactivity symptoms, and delinquency), and Total Behavior Problems (i.e., total scores on internalizing and externalizing problems).

The current study used the t-scores for internalizing and externalizing problems. T-scores were used so that internalizing and externalizing problems could be examined simultaneously across the two scales (early and school age years). T-scores also provide comparisons to gender matched norms. Means and standard deviations for each scale (separated by gender) are presented in Table 2.

Covariate Measures

Maternal medication exposure. All medications, daily dose, and self-reported adherence during pregnancy were prospectively recorded at each study visit and delivery. Medication was divided into classes (SSRI's, SSNI's, other antidepressants, mood stabilizers, typical antipsychotics, and atypical antipsychotics) and AUC was calculated for exposure to each class throughout pregnancy.

Data Analysis

The AMOS 18.0 program (Arbuckle, 2008) was used to test the structural equation models. To adjust for non-normality in the data, maximum likelihood estimation was used. Three fit statistics are reported for each model: the χ^2 index, the comparative-based fit index (CFI), and the root-mean-square error of approximation (RMSEA; Brown & Cudeck, 1993). The χ^2 index compares how closely the path coefficients in the sample model compare with what would be expected in the population. Nonsignificant χ^2 values are indicative of a good fitting model.

The CFI, an incremental index, and RMSEA (and 90 percent confidence intervals), a population-based fit index are also reported because trivial differences may inflate the χ^2 statistic. The CFI compares the sample model with the independence model yielding values ranging from 0 to 1. Values of 0.90 or greater indicate an acceptable model fit (Hu & Bentler, 1999). RMSEA tests the lack of fit between the sample model and the estimated population model covariation matrix (Kline, 2005). RMSEA values range from 0 to 1, with values less than .06 indicating an acceptable model fit (Hu & Bentler, 1999).

The first hypothesis, that maternal psychological distress during pregnancy would be positively associated child behavior problems, was tested using the models shown in Figures 1 and 2. The construct of maternal psychological distress was estimated using AUC calculations from each of the manifest variables – the CGI, the HRSD, the BDI, and the PSS. The second, third, and fourth hypotheses then built upon these initial models. The second hypothesis, that the child's HPA axis activity at six months would mediate the association between maternal psychological distress during pregnancy and child behavior problems was tested by adding HPA axis activity to the model, and examining the associations between maternal distress during pregnancy and the child's HPA axis activity, and the child's HPA axis activity and behavioral problems (Figure 3). The third hypothesis, that the association between maternal psychological distress during pregnancy and child behavior problems would be stronger in the presence of an S-allele on the serotonin transporter gene-linked polymorphism region in the child, was tested by including only the children with one or two copies of the risk allele in the model, and examining the Beta weights of this model compared to the general model (Figure 1). The fourth hypothesis, that the association between maternal psychological distress and child behavior problems would be stronger in women with lower levels of social support during pregnancy, was tested by first

dividing the participants using a median split into a "high" satisfaction and "low" satisfaction group. Each group was then tested individually, and the models were compared.

The fifth hypothesis, that the timing of the exposure to maternal distress would moderate the association between maternal distress and child behavioral outcomes was tested in similar fashion, with new models being constructed that used the manifest variables collected in the first, second, and third trimesters respectively. These models were then compared to the overall general model. The sixth hypothesis, which looked at the potential moderating effect of gender, was examined by splitting the sample by gender and running separate models for males and females. To test the mediating effect of current maternal depressive symptoms on the association between maternal distress during pregnancy and child behavior outcomes, the association between current maternal symptoms and child behavior problems were first examined. Given the significant association, current maternal symptoms was then added to the general models and the changes in the Beta weights and chi squares were examined.

Results

Preliminary Analyses. Bivariate correlations between all measures of maternal psychological distress during pregnancy were examined first. As the measures were all highly correlated (see Table 3) it was considered statistically appropriate to collapse them into a latent variable of maternal psychological distress, as described above. Additional bivariate correlations between the dependent variables and potential demographic confounds were then examined to determine if any confounding variables needed to be controlled for in the analyses.

No significant correlations between medication exposure and the dependent variables were noted (Table 4) and therefore medication exposure was not included in any of the models. Preliminary analyses were also performed to test for associations between the dependent

variables and potential demographic confounds including gender, ethnicity, years of education, parity, gravidity, marital status, and marital history (number of previous marriages) (Table 5). Males had significantly more internalizing problems than females (M = 47.50, SD = 9.9 and M = 43.90, SD = 9.9 respectively) and therefore gender was included as a covariate in all models predicting to internalizing behavior problems. Marital history was significantly related to externalizing problems (r = .15, p = .05) and was therefore included as a covariate in all models examining externalizing behavior problems.

Hypothesis 1. In order to test our first hypothesis, we examined whether maternal distress during pregnancy predicted child internalizing and externalizing problems in the context of SEM (Figures 1 and 2). The structural models predicting internalizing and externalizing problems fit well (internalizing: $\chi^2(df = 9) = 15.97$, p = .06, CFI = .979, RMSEA(90% CI) = .06(.00-.12); externalizing: $\chi^2(df = 9) = 16.88$, p = .05, CFI = .98, RMSEA = .074 (.00 - .12)). Results indicated that maternal distress significantly predicted both internalizing and externalizing behavior problems in children (β = .23, p < .01 and β = .22, p < .01, respectively).

Hypothesis 2. Next, we examined the potential mediating role of the child's cortisol level on the association between maternal distress during pregnancy and internalizing and externalizing behavior problems. Infant baseline cortisol was significantly associated with internalizing problems (r = .30, df = 85, p = .006) but not externalizing problems (r = .18, df = 85, p = .11). Infant cortisol reactivity was not associated with internalizing or externalizing problems. We therefore tested whether infant baseline cortisol acted as a mediator between maternal distress and child internalizing problems in the context of SEM. The structural model met criteria for a good fit according to two of the three fit indices (internalizing: $\chi^2(df = 8) = 19.9$, p = .06, CFI = .98, RMSEA(90% CI) = .07(.00-.13)). Results from the model revealed that

maternal distress during pregnancy did not predict infant baseline cortisol levels (β = .02, *p* =.85), but infant baseline cortisol (β = .25, *p* = .003) and maternal distress (β = .23, *p* =.006) independently predicted internalizing problems in children (Figure 3).

Hypothesis 3. To test the moderating effect of the risk allele (s) of the serotonin transporter gene, only the children with one (*n* = 39) or two (*n* = 12) copies of the risk allele were included in separate SEM models examining internalizing and externalizing behavior problems. Our hypothesis predicted that associations between maternal distress and child behavior problems should be stronger in this subsample of children. The structural models fit well (internalizing: $\chi^2(df = 9) = 8.41$, $p = .49$, CFI = 1.0, RMSEA(90% CI) = .00(.00-.15); externalizing: $\chi^2(df = 9) = 8.19$, $p = .56$, CFI = 1.0, RMSEA = .00 (.00-.15)) but indicated that maternal distress during pregnancy did not significantly predict internalizing (β =.19, *p* =.17) or externalizing (β = .23, *p* = .11) problems in this subsample. This finding does not suggest support for the moderating effect of the risk alleles of the serotonin transporter gene in the association between maternal distress in pregnancy and child behavioral outcomes.

Hypothesis 4. Prior to testing the moderator model for social support, the associations between maternal relationship satisfaction during pregnancy, measures of distress during pregnancy, and child behavior problems were examined. Relationship satisfaction was highly correlated with all measures of distress (see Table 6) and was correlated with externalizing problems (*r* = -.18, *df* =126, *p* =.04) but not internalizing problems (*r* =.15, *df* =126, *p* =.10). A median split was used to divide the sample into a "high" satisfaction (*n* = 63) and a "low" satisfaction (*n* = 64) groups. Thirty-five mother-child pairs were excluded from this analysis because of missing data. In the group of women who reported high partner satisfaction, the model showed adequate fit (internalizing: $\chi^2(df = 9) = 6.57$, $p = .68$, CFI = 1.0, RMSEA(90% CI)

= 1.0 (.00-.12); externalizing: $\chi^2(df = 9) = 13.50$, $p = .14$, CFI = .96, RMSEA(90% CI) = .09 (.00-.18)) however there was not a significant association between maternal distress during pregnancy and internalizing problems ($\beta = .15$, $p = .21$) or externalizing problems ($\beta = .20$, $p = .15$). In the group of women who reported low partner satisfaction, the model again fit well (internalizing: $\chi^2(df = 9) = 10.75$, $p = .29$, CFI = .98, RMSEA(90% CI) = .06(.00-.16); externalizing: $\chi^2(df = 9) = 12.37$, $p = .19$, CFI = .98, RMSEA(90% CI) = .07(.00-.17)) and maternal distress during pregnancy significantly predicted internalizing ($\beta = .37$, $p = .03$) and externalizing ($\beta = .26$, $p = .04$) problems. Goodness of fit tests showed that this model significantly differed from the overall models (see Hypothesis 1), suggesting the model with social support was a stronger model.

Hypothesis 5. To examine the role of timing of maternal distress during pregnancy, new models were constructed including maternal distress measures calculated separately for each trimester of pregnancy. As shown in Table 7, the first trimester model for externalizing problems poorly fit the data, but the models for the first trimester internalizing problems, second trimester (internalizing and externalizing) and third trimester (internalizing and externalizing) demonstrated adequate fit. Results from the structural equation models indicate that maternal distress during the second trimester did not predict child externalizing problems ($\beta = .12$, $p = .16$), and only predicted child internalizing problems at a trend level ($\beta = .15$, $p = .06$). Maternal distress during the third trimester significantly predicted child internalizing ($\beta = .24$, $p = .005$) and externalizing problems ($\beta = .28$, $p = .002$). Goodness of fit tests showed that the third trimester structural equation models significantly differed from the overall models (see Hypothesis 1) for both internalizing and externalizing problems, suggesting the third trimester models were statistically stronger models.

Hypothesis 6. As indicated in the preliminary analyses, there was a significant gender difference for internalizing but not externalizing problems (Table 5). Gender was included as a covariate in all of the internalizing models, but did not significantly change any of the results. Attempts to split the sample by gender and run separate models for males and females resulted in poorly fitting models in all cases. Due to this, we were unable to reliably test for the potential moderating impact of gender in our predictive models.

Hypothesis 7. To examine the role of current maternal depressive symptoms in the association between maternal distress during pregnancy and child internalizing and externalizing behavior problems, a new structural model was constructed for each child outcome as shown in Figures 4 and 5. Both models fit well (internalizing: $\chi^2(df = 13) = 20.13$, $p = .09$, CFI = .98, RMSEA(90% CI) = .06(.00-.11); externalizing: $\chi^2(df = 13) = 21.37$, $p = .07$, CFI = .98, RMSEA= .06 (.00-.10)). There was a very strong association between maternal distress during pregnancy, and current depressive symptoms and current depressive symptoms and child behavior problems. However, with current depressive symptoms in the model, the association between maternal distress during pregnancy and internalizing or externalizing problems was no longer significant, indicating that current maternal depression fully mediates the association between maternal distress during pregnancy and child behavior problems.

Post-hoc analyses. In order to better understand the magnitude of the mediation described in hypothesis 7, current maternal depressive symptoms were added to the strongest models (3rd trimester). While both of the models fit well (internalizing: $\chi^2(df = 13) = 14.74$, $p = .32$, CFI=.99, RMSEA(90% CI)= .03(.00-.09); externalizing: $\chi^2(df = 13) = 19.35$, $p = .11$, CFI=.98, RMSEA= .06(.00-.10)), maternal distress did not predict internalizing or externalizing problems ($\beta = .06$, p

= .59 and β = .16, p = .16) when current maternal depressive symptoms was included as a mediator term.

The impact of the child's age was also examined in post-hoc analyses. Age was significantly associated internalizing problems (r = .22, p = .006) but not externalizing problems (r = .12, p = .14). The addition of age as a covariate to the internalizing models resulted in poor fit, suggesting that its inclusion was not useful in terms of prediction. To further examine the impact of age, each of the models was run with only the younger group of children (ages 1-5). There was no difference in the associations between the independent and dependent measures in these models versus those that included all of the children in the follow up sample.

Discussion

The goal of this study was to examine the impact of maternal psychological distress during pregnancy on child behavioral outcomes as well as the potential mediating and moderating effects of biological, psychological, and social factors on the maternal distress-child behavior problem relationship. Maternal distress was conceptualized not as the presence of a set of symptoms specific to a single disorder, but rather as a compilation of self-reported and clinician-rated measures that spanned across diagnostic categories and that were measured throughout pregnancy, thereby constructing a latent variable that provided a more comprehensive measure of the distress experienced by the participant.

The overarching hypothesis of the study, that maternal distress would predict child internalizing and externalizing behaviors, was supported. Given the robust evidence linking prenatal mood disturbances with behavioral/mood problems in offspring, this finding was not surprising and is consistent with studies that have independently examined the impact of prenatal depression (e.g., Carter et al., 2001; Luoma et al., 2001), anxiety (e.g., O'Connor et al., 2002;

2003; Van den Bergh et al., 2004; 2006) and stress (e.g., Gutteling et al., 2005; Rodriguez & Bohlin, 2005) on child behavior outcomes.

This study added to the literature by examining potential mediators and moderators of the prenatal maternal distress-child outcome relationship. As reviewed in the introduction, there has been considerable interest in understanding the role of the endocrine system as a pathway of intergenerational transmission, and the impact of maternal mood on the fetal programming of the HPA axis. While various studies have examined the associations between maternal mood during pregnancy and fetal behavior (Sandman et al., 1999), maternal cortisol during pregnancy and neonatal cortisol (Lundy et al., 1999), and infant cortisol and infant behavior (Field & Diego, 2008), this is one of the first studies to take the next step of examining the child's HPA axis activity as a potential mediator of the association between maternal distress during pregnancy and child behavioral outcomes. Importantly, we did not find support for this hypothesized mediator effect. Specifically, there was no association between infant cortisol reactivity and child behavior problems, and although baseline cortisol independently predicting internalizing problems, it was unrelated to maternal distress during pregnancy and therefore did not mediate the association between distress during pregnancy and child internalizing problems.

Given the abundant animal literature (e.g., Seckl & Meaney, 2004) and the emerging human literature (e.g., Gitau et al., 2001; O'Connor et al., 2005) supporting fetal programming of the HPA axis, the lack of association between maternal distress during pregnancy and infant cortisol measures was unexpected. In the original study examining maternal depression and infant cortisol (of which a subset of our participants with infant cortisol data also completed; Brennan et al., 2008) peripartum exposure to maternal depression and comorbid maternal anxiety was strongly associated with cortisol reactivity. Therefore, it is possible that our lack of findings

was due to a more restricted clinical sample. It will be important, therefore to examine this question in larger, more representative samples in the future. Although not the main focus of this study, the association between baseline cortisol and internalizing disorders is noteworthy. Findings from several studies have suggested that elevated baseline cortisol levels are associated with psychosocial disturbance and/or risk (as reviewed in O'Connor et al., 2005) and our finding could be interpreted to mean that baseline cortisol in infancy may be an early marker of risk for later child behavior problems. However, further research aimed at directly examining the replicability of this finding is necessary before any conclusions can be drawn.

This study also attempted to assess the potential impact of genetic influences on the association between maternal distress during pregnancy and child behavioral outcomes. While numerous studies in the adult literature have focused on the effect of specific candidate genes and risk alleles, this has only very recently been examined within the child literature. The findings from the current study did not support the hypothesis that the risk allele of the serotonin transporter gene would moderate the association between maternal distress during pregnancy and child behavioral outcomes. The findings differ from those of Pluess and colleagues (in press) who observed a significant association between the 5-HTTLPR short allele and negative infant emotionality only in those infants whose mothers had reported high levels of prenatal anxiety. It is possible that the effects noted by Pluess and colleagues (In press) are very specific to negative emotionality, and do not generalize to broadband behavioral categories such as internalizing and externalizing behavior problems. The differences in findings across studies may also be explained by the difference in sample sizes between the current study (n = 82) and Pluess et al. (n = 1513). Because our sample size was quite limited, it is likely that it was not sufficient to adequately assess for the hypothesized gene by environment interaction. Therefore, attempts to

examine this hypothesis in a larger sample would be needed before a more definitive conclusion could be drawn.

We also investigated social support (as measured by relationship satisfaction) as a moderator of the association between maternal distress and child behavioral outcomes, predicting that the association would be stronger in women with low levels of social support. While it has been well established in the literature that there are strong associations between social support and psychiatric distress during pregnancy, there are very few studies that extend these findings to examine the impact on the child. The current study found statistical support for the moderating effect of social support on the association between maternal distress and child behavioral outcome; however these results should be interpreted with some level of caution given the high correlations between maternal distress and low social support. Visual examination of the data indicated that very few women with high levels of social support had high levels of distress. It may be the case that the weaker associations between maternal prenatal distress and child behavior problems noted for women with high social support are due to a restricted range of the distress measures in this subgroup. Nevertheless, the findings clearly suggest that women with low levels of support have more distress during pregnancy, and that this distress is associated with child behavioral outcomes.

In this study we also examined the role of gestational timing in the association between prenatal maternal distress and child behavioral outcome. The experimental animal literature has suggested that maternal distress occurring during late pregnancy has the strongest impact on the fetuses HPA axis development (Welberg & Seckle, 2001) however these findings have not been consistently replicated in the human literature (e.g., O'Connor et al., 2002; Van den Berg & Marcoen, 2004). One of the most likely reasons for the lack of consistent findings in humans is

that many studies are either conducted retrospectively and/or only collect data at a few time points during pregnancy. The current study assessed maternal distress prospectively throughout pregnancy and we were therefore able to examine potential differences in the strength of the association between maternal distress occurring in the first, second, and third trimester respectively, and child behavioral outcomes. The findings from the current study were similar to those in the animal literature and those noted by O'Connor and colleagues (2002, 2003), suggesting that maternal distress during the third trimester had the strongest association with internalizing and externalizing behavior problems. While Van den Bergh & Marcoen (2004) focused on the finding that maternal anxiety during early pregnancy was the strongest predictor of child attentional problems, their results indicated that maternal anxiety during late pregnancy was associated with child internalizing problems. While more prospective research is still needed to replicate the findings from the current study, the accumulated findings in the literature suggest that maternal distress during late pregnancy has the strongest association with child behavior problems.

In this study we also attempted to examine the impact of gender on the association between maternal distress during pregnancy and child behavioral outcomes. The fetal programming hypothesis would suggest that male fetuses are more vulnerable to the effects of maternal distress during pregnancy compared to female fetuses (Schneider & Moore, 2000), although the gender differences with regards to child behavioral problems are inconclusive. While some studies have noted more externalizing problems in boys exposed to maternal depression and anxiety (e.g., Carter et al., 2001, O'Connor et al., 2002; Van den Bergh et al., 2006) others found no gender differences (e.g., Luoma et al., 2001; Van den Bergh & Marcoen

2004). In the current study, males had significantly more internalizing problems than females but the moderating effect of gender could not be accurately tested due to statistical constraints.

Finally, we examined the impact of current maternal depressive symptoms on the relationship between maternal distress during pregnancy and child behavioral outcomes. These analyses yielded perhaps some of the most interesting findings in our study. Current maternal depressive symptoms were highly correlated with all measures of distress during pregnancy and with the latent construct of distress, affirming the chronic nature of many of the symptoms of distress used in this study. When current maternal distress was added to the structural equation models, it not only became the strongest predictor of child behavioral outcomes, but also fully mediated the association between distress during pregnancy and child behavioral outcomes. The implications of this finding are discussed in detail below.

Significance of Antenatal Factors

While the results of this study add to the growing body of literature showing that maternal distress during the prenatal period can have lasting effects on the psychological development of offspring, many of the findings are not well explained by the fetal programming hypothesis, thus requiring additional theoretical models of developmental processes. Most significant was the finding that when current maternal symptoms were included in the models, prenatal maternal distress was no longer associated with child behavioral outcomes. The majority of studies examining the fetal programming hypothesis in association with child outcomes included measures of postpartum distress, but essentially ignored the role of concurrent maternal distress in predicting outcome. Out of the eight prospective studies examining prenatal maternal distress and child outcomes, all but one (Rodriguez & Bohlin, 2005) included a measure of postnatal maternal distress. Five of the studies included measures of postnatal maternal distress

and reported the results of prenatal maternal distress on child outcome measures after "controlling" for the impact of postnatal distress. However, the majority of the measures of postnatal maternal distress were completed during the first postpartum year, with the child outcome measures completed years later. O'Connor et al., (2002) had the smallest window between postnatal distress and child outcome measurements, with the last maternal mood measure completed at 33 months postpartum and the child behavioral outcome measures completed when the child was 48 months. Other studies showed much greater discrepancies such as Van den Bergh (2004; 2006) who measured maternal mood 28 weeks after birth and child outcome at 8 years and 13 years respectively. Only two studies included measures of maternal distress at the time of the child follow-up (Carter et al., 2001 and Gulteling et al., 2005). In each of these studies, the impact of postnatal distress on child outcome was as strong or slightly stronger than the impact of prenatal distress. Neither study reported the associations between prenatal distress and child outcome after controlling for concurrent distress, nor did they examine the mediating impact of concurrent distress on the association.

In one of the only studies of its kind documented in the literature, Rice and colleagues (2007) used a 'prenatal cross-fostering' design in which pregnant mothers were related or unrelated to their child as a result of IVF, and examined the link between prenatal maternal stress, current maternal anxiety and depression and offspring outcome (symptoms of anxiety, antisocial behavior, and ADHD). The results of this study indicated that associations between prenatal stress and offspring anxiety and antisocial behavior were observed in both the related and unrelated mother-child dyads, suggesting that prenatal environmental factors, rather then heritability, were the causal mechanism. Importantly, this study also examined the impact of current maternal anxiety/depression and found that when entered into the model, current

maternal anxiety/depression accounted for the association between prenatal stress and offspring anxiety, findings very similar to the current study.

While the results of our study do not entirely negate the fetal programming hypothesis, they do underscore the importance of systematic postnatal monitoring of participants, so that the impact of postnatal factors can also be assessed. At the very least, studies that are measuring child behavioral outcomes should include a concurrent measure of maternal distress, preferably across similar constructs to those measured during pregnancy. Our findings also underscore the need for further clinical research on the development and utility of clinical interventions aimed at reducing problem behaviors in children. If our findings are replicated, specific interventions focused on current maternal distress may provide an avenue for decreasing child behavior problems associated with prenatal stress. As recent studies have noted, interventions aimed at decreasing current maternal distress may positively impact the child's behavior, without requiring direct intervention for the child (Pilowsky, Wickramaratne, Talati, Tang, Hughes, Garber et al., 2008).

Limitations of the Current Study

The current study was hampered by several methodological limitations. Perhaps the most significant limitation of the study was the sample size, which was smaller than anticipated due to the number of potential participants lost to follow-up. Structural equation modeling requires a larger sample size that most other statistical techniques, therefore making some of our moderator hypotheses difficult to test. Given that the use of SEM was a significant strength of the study, future studies should look to replicate these findings with a larger sample size. Another limitation of the study was the lack of a control group without a lifetime history of mental illness. As a history of maternal mental illness has been shown to impact infant HPA axis activity

(Brennan et al., 2008), a control group would allow for the examination of the potentially additive impact of lifetime mental illness.

Measurement difficulty was also a limitation of the current study. The study did not include a specific anxiety measure in the prenatal measures of maternal distress. As reviewed previously, prenatal anxiety has been shown to strongly impact child behavioral outcomes. While some symptoms of anxiety were assessed through other prenatal measures (i.e., the CGI), the addition of an anxiety measure may have strengthened the findings from this study. Along similar lines, the only measure of social support during the prenatal period was focused on relationship support, which thereby excluded women who were not in a relationship with a significant other. Additionally, only having one measure of current maternal mood at follow-up meant that we were unable to construct a comprehensive model of current maternal distress. Given the noted impact of current maternal symptoms in this study, along with those reported by Rice and colleagues (2007), a comprehensive model of current maternal distress would have improved the generalizability of the findings. Similarly, our study only included one measure of child outcome, which was completed by the child's mother. There is a possibility that the mother's current symptomatology could have impacted her perception of her child's behavior, and having multiple reporters (such as teachers, fathers) would have allowed us to examine the findings for potential bias.

Strengths of the Current Study

The limitations reviewed above are offset by several strengths of the study. The first is the unique way in which maternal distress during pregnancy was conceptualized. The standard practice within the field is to conceptualize "distress" as a single set of symptoms (such as depression), control for any potential comorbid symptoms (such as anxiety), and use self-report

questionnaires as the primary tool of measurement. The drawback to this technique is that it only provides a partial picture of the distress being experienced by the mother, especially if other aspects of distress are being statistically controlled for. This technique also makes it very difficult to generalize these findings into clinical settings, again due to issues of comorbidity. The measure of distress used in this study also took advantage of multiple measurement points of distress during pregnancy. Instead of collapsing the individual measures of distress into an average score, the AUC was calculated for each measure, providing a cumulative index of each aspect of distress. We also used SEM to construct a latent variable of distress comprised of a variety of self-report and clinician-rated measures spanning across diagnostic categories and measured throughout pregnancy; this latent variable provides a good approximation of the unique distress experienced by each participant.

The second major strength of the current study was its prospective design. Because participants in the current study had previously participated in a longitudinal study during pregnancy, prospective prenatal stress data was available. Each participant had multiple clinic visits during pregnancy that included meetings with a research assistant and a study psychiatrist, allowing for very detailed information to be gathered about mood symptoms and any changes in medication. This meant that we were not required to rely on retrospective recall, which increased the accuracy of our data.

Given the inconclusive findings in the literature regarding specific behavioral problems in children prenatally exposed to maternal distress, two measures of child behavior problems were used in this study, providing information about both internalizing and externalizing problems. This approach proved to be very fruitful, as several of the mediators and moderators had effects specific to either internalizing or externalizing problems. Internalizing problems were

related to baseline cortisol and gender, whereas externalizing problems were related to social support during pregnancy. Both internalizing and externalizing problems were associated with overall distress, especially in the third trimester, and the association between maternal distress and internalizing/externalizing problems was mediated by current maternal distress. Whereas the literature has reported prenatal distress is mainly related to externalizing behaviors, our findings demonstrated the importance of also including measures of internalizing behavior problems, as these problems were often just as strongly related to prenatal distress in this sample.

Clinical Implications

The findings from the current study have significant clinical implications for mothers and their children, specifically in the development of innovative screening procedures and intervention development and delivery. Children are routinely referred to their pediatrician or mental health professionals for behavioral concerns. The findings from the current study suggest that when children are referred for such problems, it may be clinically appropriate for health care providers to not only assess the child, but also screen parents for current symptoms of psychosocial distress. Understanding the current psychosocial functioning of the parents could have a significant impact on treatment recommendations provided to the family, by helping elucidate the potential origin of the child's behavior problem. If parental distress was found to be the precipitant to the child's behavior problem, then the 'treatment' for the child would be to provide resources for the parent. Research has recently demonstrated that the treatment of maternal depression significantly decreases incidents of problem behavior in children, without requiring any additional intervention for the child (Pilowsky et al., 2008). An intervention focused on treating parental symptomatology is very different than the treatment recommendations that may be offered that focus on the child, such as medication.

Within the literature there are many well designed and empirically supported interventions aimed at increasing social support during pregnancy. Large randomized control trials have shown that these interventions are both cost effective and efficient, and can reduce the rate of low birth weight in high-risk populations (Norbeck, DeJoseph, & Smith, 1996). Based on the strong relationship between maternal distress and social support during pregnancy, it is likely that interventions increasing social support may also have the secondary effect of decreasing maternal distress. In addition, our findings concerning the moderating influence of social support suggest that the development of interventions aimed at increasing social support during pregnancy could also decrease the likelihood of later child behavior problems linked to prenatal distress.

Future Directions

While this study adds to a growing literature examining the association between perinatal maternal distress and child behavior problems, continued research is needed to replicate and extend the findings. Given the significant impact of current maternal symptoms on the association between maternal distress during pregnancy and child behavior outcomes, future research needs to consider other concurrent psychosocial stressors that could also contribute to child behavior problems. In the literature examining the impact of maternal mood on child behavior problems, the role of the father (or other adult caretakers) is often ignored. If child behavior is significantly impacted by the mother's current symptoms, then it likely that it is also impacted by the symptoms of other adult caretakers. The research on the impact of current maternal functioning on child behavior problems needs to be extended to include other adults in the child's life, whether it is a father, stepfather, or other parental figure. Limited research has demonstrated significant associations between paternal postnatal depression and child behavior

problems at 3.5 years, along with an increased risk for conduct-related problems in boys (Ramchandani, Stein, Evans, & O'Connor, 2005), but the impact of paternal mood on child behavior problems has not received nearly the attention that maternal mood has.

One of the most unique features of the current study was its dimensional approach to the conceptualization of maternal distress, as oppose to the more categorical approach taken by the majority of research in this area. The field of psychology has long recognized the limitations associated with the categorical approach to diagnostic classification, and is beginning to incorporate dimensional elements into the classification system with the development of the newest edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)* (Brown & Barlow, 2009). As the field continues to incorporate dimensional elements into the clinical understanding of psychology, it is critical that research also reflects this shift. Future research would benefit a move away from the focus on diagnostic categories (e.g., the impact of prenatal depression) towards more a more dimensional, construct-based focus (e.g., the impact of prenatal distress).

Conclusions

It is well established in the literature that maternal emotional functioning during pregnancy can have a lasting impact on the development of the fetus and that this impact can last into late childhood and possibly beyond. This study expanded on the current literature by examining the impact of maternal distress during pregnancy on child behavior problems using statistical techniques to model a latent factor of maternal distress that was more representative of the "true" levels of distress experienced by women during their pregnancies. Maternal distress during pregnancy was significantly associated with child behavior problems and this relationship was moderated by maternal social support during pregnancy and mediated by current maternal

symptoms of depression. This study not only reflects the shift in the field of psychology from categorical conceptualization towards a more dimensional conceptualization, but also underscores the importance of taking a wider view when examining the impact of maternal distress on child behavior by including current maternal symptomatology into the models. The findings from this study have clinical applications in development of screening procedures and interventions. While future research on using a more dimensional approach to examining the association between maternal psychosocial distress during and after pregnancy and child behavior problems are needed, this study is an important first step.

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Table 1

Demographic differences in participants who participated in the follow-up study

	Followed Up *M* (*SD*)	Not Followed Up *M* (*SD*)	*t*	*df*
Education	16.72 (1.61)	16.03 (1.96)	3.44***	329
Maternal Age	34.59 (4.08)	34.21 (4.60)	0.78	330
CGI	71.45 (29.09)	77.80 (33.12)	1.46	217
HRSD-17	408.64 (166.98)	447.73 (184.25)	1.93	302
BDI	407.72 (293.35)	488.98 (299.63)	2.49**	325
PSS	976.94 (346.36)	1068.14 (330.05)	2.41**	319
	% (n)	% (n)	χ^2	*df*
Pregnancy			11.75**	2
Planned	70 (114)	51 (91)		
Unplanned	15 (24)	23 (42)		
Unknown	15 (24)	26 (46)		
Race			3.45	3

White	95 (154)	94 (168)		
Other	2.5 (4)	2.8 (5)		
Black	.5 (1)	2.8 (5)		
Asian	2 (3)	0.6 (2)		
Marital Status			5.74	3
Never Married	1.8 (3)	6 (10)		
Married	95 (155)	93 (162)		
Separated	.6 (1)	.6 (1)		
Divorced	1.8 (3)	.6 (1)		
Gender			0.29	1
Male	51 (83)	50 (90)		
Female	49 (79)	40 (89)		
Neonatal Complications			3.14	2
Yes	58 (89)	55 (83)		
No	42 (64)	43 (66)		
Unknown	0 (0)	2 (3)		
Primary Lifetime Diagnosis			.251	1
Mood	82 (134)	82 (146)		
Anxiety	17 (28)	18 (33)		
Somatoform	.6 (1)	0 (0)		

*$p < .05$. ** $p < .01$. *** $p < .001$

Table 2

Child behavior scores by gender and age

	Males	Females
	M (*SD*)	*M* (*SD*)
Early Years (*n* = 138)		
Internalizing T-Score	46.85 (9.71)	43.77 (10.08)
Externalizing T-Score	45.15 (10.56)	44.30 (9.02)
School Age (*n* = 24)		
Internalizing T-Score	50.50 (10.19)	44.75 (8.29)
Externalizing T-Score	52.50 (11.77)	46.63 (8.36)

Table 3

Inter-correlation between measures of maternal distress during pregnancy

AUC Distress	1	2	3
1. CGI	--	--	--
2. HRSD-17	.71**	--	--
3. BDI	.68**	.75**	--
4. PSS	.51**	.67**	.75**

*$p < .05$. ** $p < .01$. *** $p < .001$

Table 4

Correlation between weeks of medication exposure by class and child behavioral outcomes

	Internalizing Problems	Externalizing Problems
SSRI	.04	-.10
SNRI	.13	.10
Bupropion	.07	.13
Tricyclic	.09	-.16
Anti-epileptic	-.07	-.05
Atypical Antipsychotics	-.03	.01
Typical Antipsychotics	-.05	-.10
Hypnotics	-.06	-.13
Benzodiazepines	.05	.01

*$p < .05$. ** $p < .01$. *** $p < .001$

Table 5

Association between child behavioral outcomes and potential demographic confounds

	Internalizing Problems		Externalizing Problems	
	r		*r*	
Education	-.13		-.1	
Maternal Age	-.13		-.15	
Times Married	.07		.16*	
	M (*SD*)	*F* (df)	*M* (*SD*)	*F* (df)
Pregnancy		2.45		.74
		(2, 161)		(2, 161)
Planned	44.76 (9.6)		45.30 (9.9)	
Unplanned	49.58 (10.1)		47.88 (10.5)	
Unknown	46.67 (11.1)		44.58 (10.7)	
Race		1.07		2.78
		(3, 161)		(3, 161)
White	45.50 (9.9)		45.11 (10.0)	
Other	48.75 (13.9)		55.25 (10.5)	
Black	-		-	
Asian	55.33 (7.4)		57.33 (2.8)	
Marital Status		0.32		0.14
		(3, 161)		
Never Married	48.67 (6.3)		44.00 (5.6)	(3, 161)

	Married	45.62 (19.1)	45.53 (10.3)	
	Separated	-	-	
	Divorced	50.33 (10.1)	48.00 (5.3)	
	Widowed	-	-	
Gender		5.41*		1.55
		(1, 160)		(1, 160)
	Male	47.50 (9.9)	46.52 (11.2)	
	Female	43.87 (9.9)	44.53 (8.9)	
Neonatal Complications		1.20		0.06
		(1, 152)		(1, 152)
	Yes	46.60 (10.1)	45.55 (9.2)	
	No	44.78 (10.3)	45.97 (11.3)	

*$p < .05$. ** $p < .01$. *** $p < .001$

Table 6

Associations between relationship satisfaction and maternal distress during pregnancy

AUC Distress	Relationship Satisfaction
CGI	-.45**
HRSD-17	-.47**
BDI	-.43*
PSS	-.42*

*$p < .05$. ** $p < .01$. *** $p < .001$

Table 7

SEM fit indices for trimester models

	Internalizing			Externalizing		
	χ^2 (*df*=9)	CFI	RMSEA (90% CI)	χ^2 (*df* =9)	CFI	RMSEA (90% CI)
First Trimester	15.40	.98	.07(.00-.12)	17.59*	.97	.07(.01-.13)
Second Trimester	15.75	.98	.07(.00-.12)	13.80	.99	.06(.00-.11)
Third Trimester	7.92	1.0	.00(.00-.08)	12.50	.99	.05(.00-.11)

*$p < .05$. ** $p < .01$. *** $p < .001$

Figure 1.

Association between maternal distress and internalizing problems

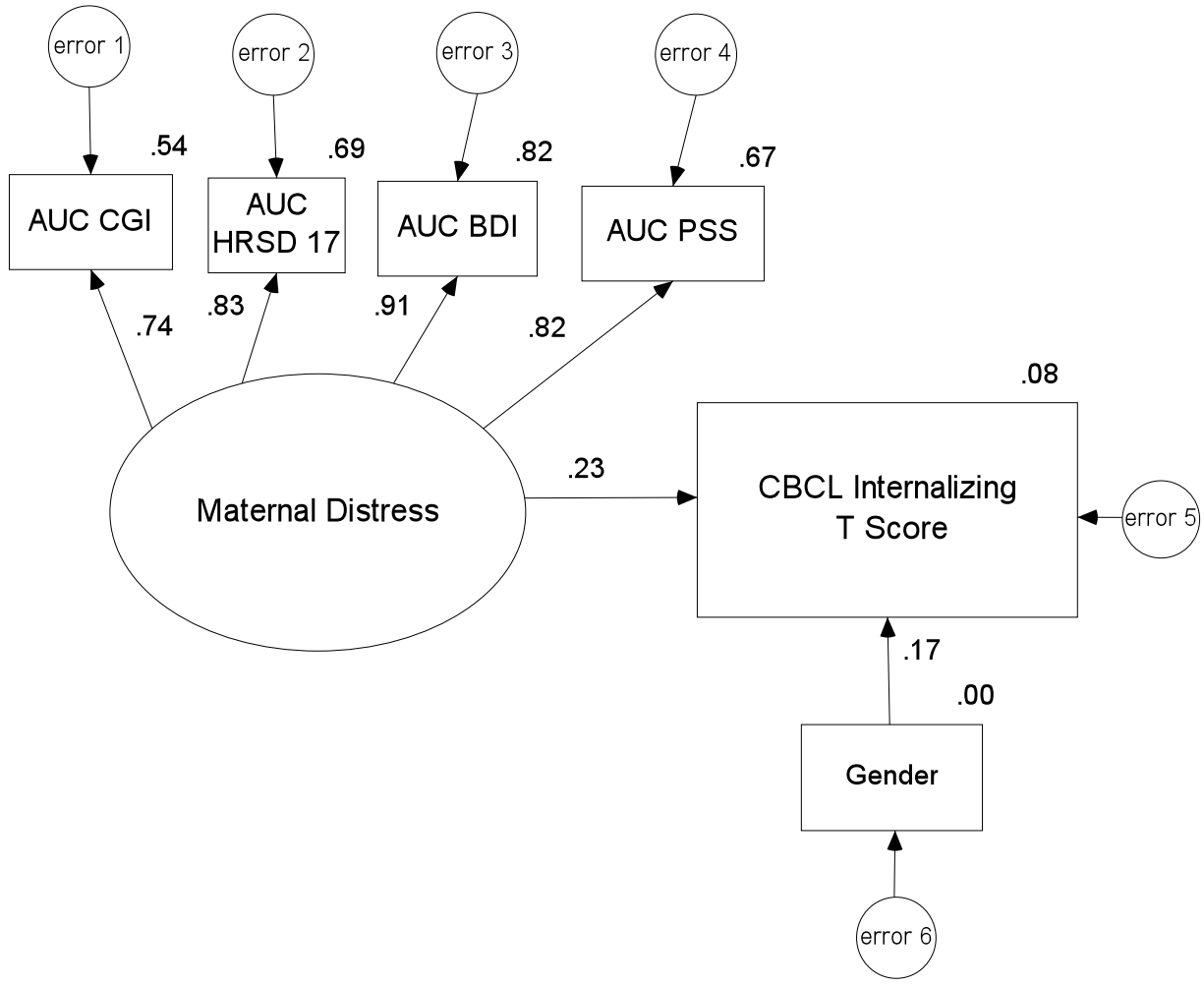

Figure 2.

Association between maternal distress and externalizing problems

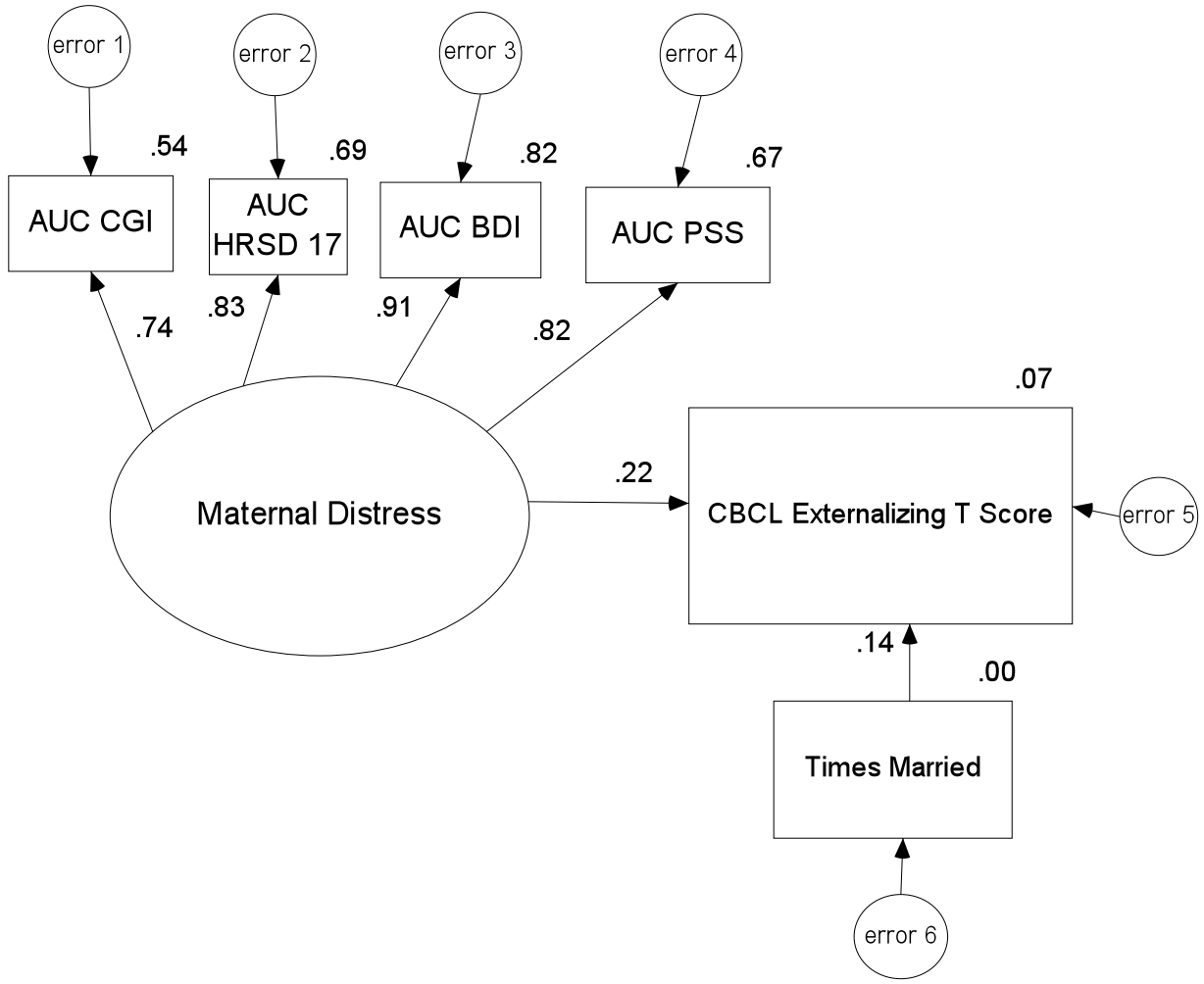

Figure 3.

Impact of infant cortisol on the association between maternal distress and internalizing problems

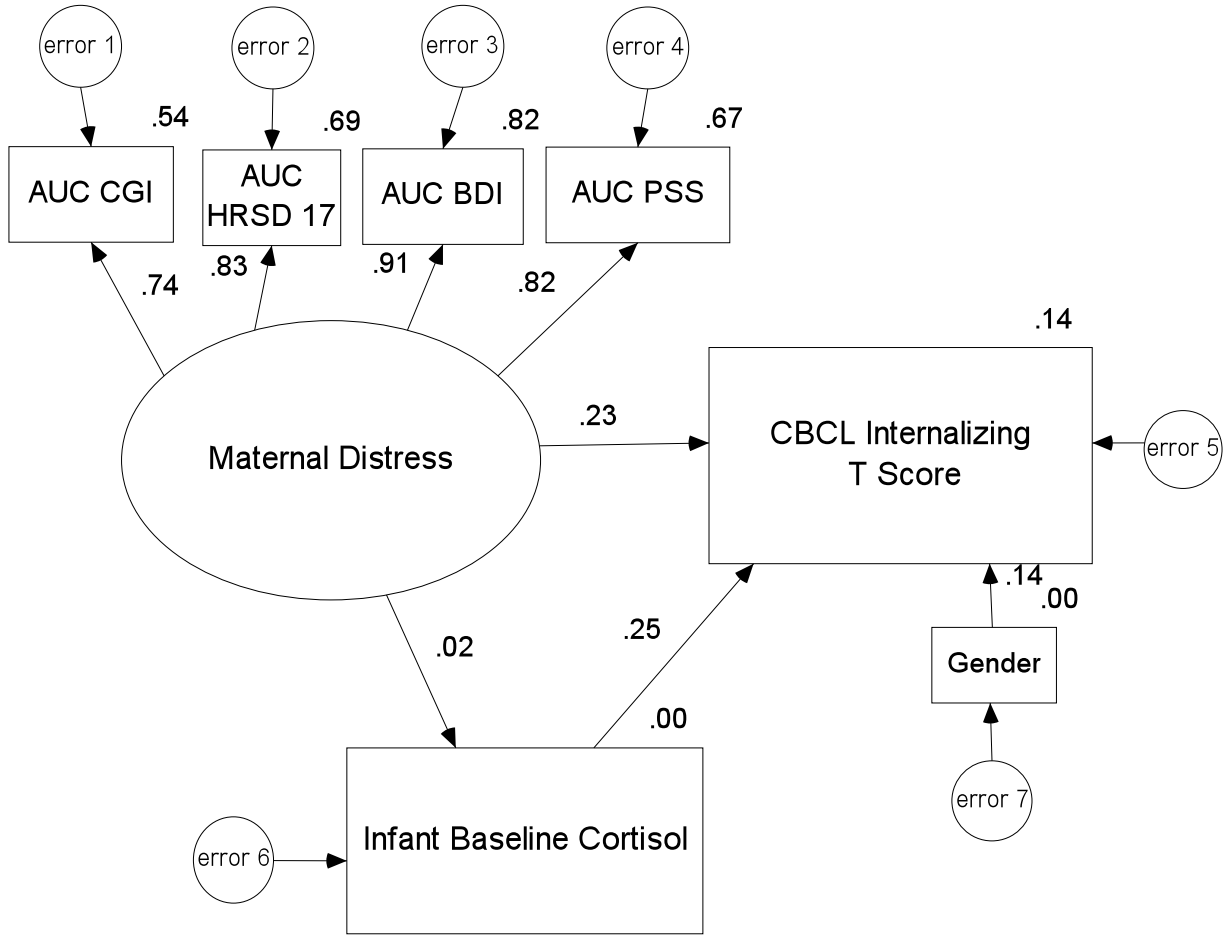

Figure 4.

Impact of current maternal depression on the association between maternal distress during pregnancy and internalizing problems

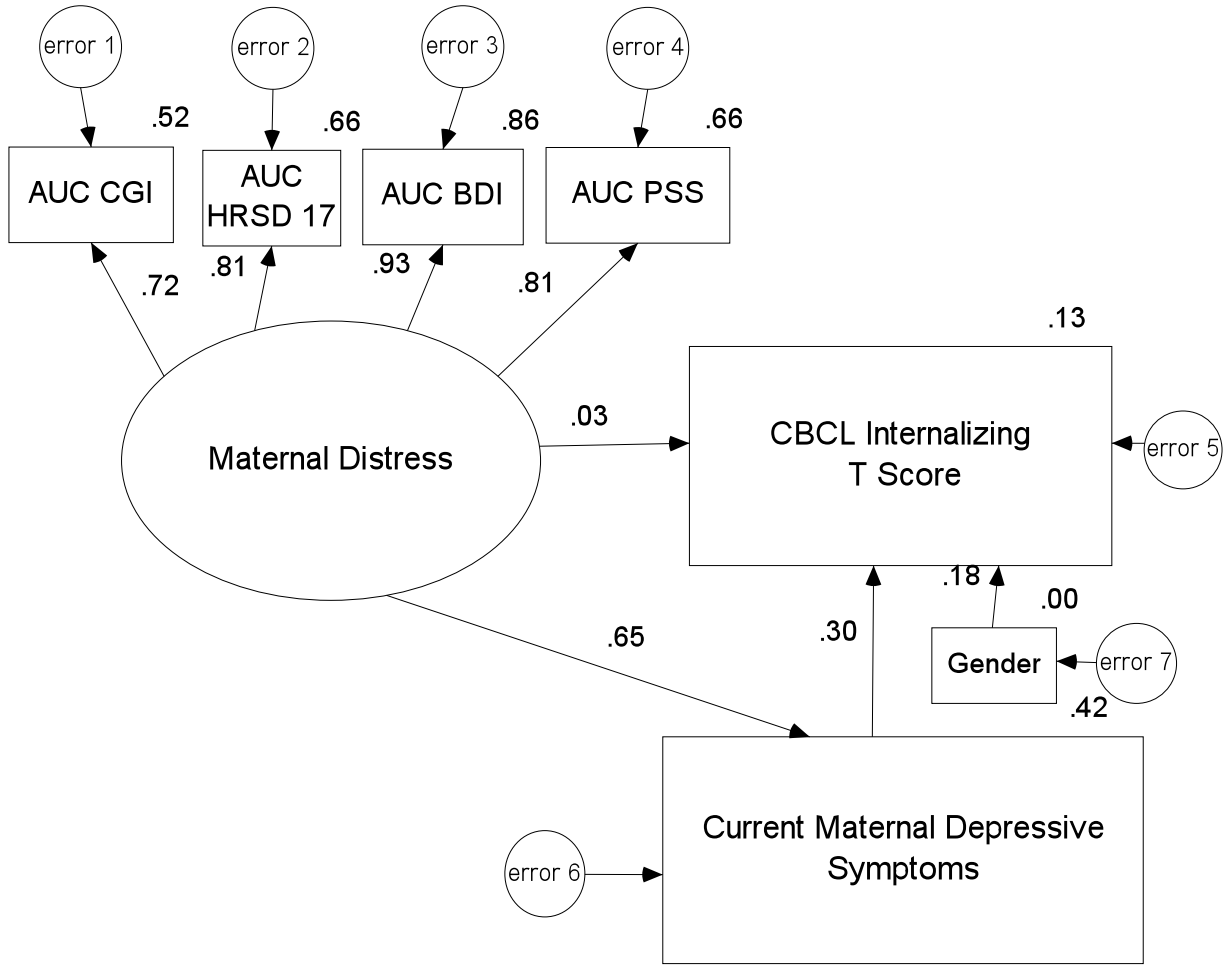

Figure 5.

Impact of current maternal depression on the association between maternal distress during pregnancy and externalizing problems