Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Melissa Engel 7-3-21

Date

Intergenerational Impacts of Maternal Stress on Early Childhood Atopy in Black Americans:

Risk and Protective Factors

By

Melissa Lauren Engel

Master of Arts

Psychology

Patricia A. Brennan, Ph.D.
Advisor

Robyn Fivush, Ph.D.
Committee Member

Sherryl H. Goodman, Ph.D.
Committee Member

Accepted:

_____

Lisa A. Tedesco, Ph.D.
Dean of the James T. Laney School of Graduate Studies

_____

Date

Intergenerational Impacts of Maternal Stress on Early Childhood Atopy in Black Americans: Risk and Protective Factors

By

Melissa Lauren Engel
M.A., University of Minnesota, 2019
B.A., Emory University, 2017

Advisor: Patricia A. Brennan, Ph.D.

An abstract of
A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
In partial fulfillment of the requirements for the degree of Master of Arts in Psychology
2021

Abstract

Intergenerational Impacts of Maternal Stress on Early Childhood Atopy in Black Americans: Risk and Protective Factors

By Melissa Lauren Engel

Black children are disproportionately affected by atopic diseases (i.e., atopic dermatitis, allergic rhinitis, asthma, and food allergies), with health disparities present in early life. Studies in White samples suggest that maternal stress confers risk for offspring atopy, yet little is known about these relationships in Black populations. This study seeks to (1) examine the relationship between self-reported and physiological indicators of maternal stress and offspring atopy and (2) explore warm and responsive caregiving as a potential protective factor in Black Americans. A sample of 179 Black mother-child dyads of varying socioeconomic status participated in a prospective longitudinal study. Mothers completed self-reports of childhood trauma, prenatal stress, postnatal stress, and physician diagnosis of offspring atopy; provided blood samples to assess physiological responses to chronic stress exposure; and participated in a behavioral task with their infant. Maternal self-reports of childhood trauma, prenatal stress, and postnatal stress were not associated with offspring diagnosis of atopy by 2-3 years of age. Mothers who produced a smaller inflammatory response during pregnancy were more likely to have an offspring with atopy by 2-3 years of age. Warm and responsive parenting demonstrated a protective effect; the positive association between maternal stress and offspring atopy was less apparent in cases of mother-child interactions characterized by high levels warm and responsive parenting. Failure to replicate previous findings suggests that the maternal stress-offspring atopy relationship is complex. Future studies must examine the unique stressors in Black Americans, as well as caregiving as a potential protective factor.

Intergenerational Impacts of Maternal Stress on Early Childhood Atopy in Black Americans:

Risk and Protective Factors

By

Melissa Lauren Engel
M.A., University of Minnesota, 2019
B.A., Emory University, 2017

Advisor: Patricia A. Brennan, Ph.D.

A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
In partial fulfillment of the requirements for the degree of Master of Arts in Psychology
2021

Table of Contents

List of Tables

Introduction

Stress experienced early in development is associated with a plethora of chronic diseases across the lifespan (Miller et al., 2011). Importantly, the prevalence of prenatal and early life stress, as well as many chronic diseases, is heightened in Black youth (Daya & Barnes, 2019). Rates and outcomes of childhood atopic diseases (i.e., atopic dermatitis, allergic rhinitis, asthma, and food allergies) highlight these health disparities. For instance, compared with White children, Black children are twice as likely to have asthma (CDC, 2018) and six times as likely to die of an asthma attack (Chen Arroyo, 2017). Likewise, early childhood atopic dermatitis is more likely to remain persistent among Black youth (Kim et al., 2019), and food allergy prevalence in Black children has risen at double the rate of that of White children over the past two decades (Keet et al., 2014). Racial disparities in atopic diseases appear as early as two years of age and are not explained by socioeconomic factors alone nor additional factors commonly associated with offspring atopy (e.g., parental atopy, tobacco exposure, birth weight, breastfeeding, environmental allergen exposure), suggesting that the etiology of atopy may be shaped by biological or environmental factors during, and perhaps even prior to, gestation (Wegienka et al., 2012). Although a plethora of biological and environmental risk factors for atopy have been identified (for review, see Halken, 2004), few studies have examined maternal stress as a potential risk factor. However, accumulating evidence supports a relationship between maternal stress and offspring atopy, whereby stress during sensitive periods in fetal development may influence the child's developing immune system (Rosa et al., 2018). Despite this general association, little is known about the type of maternal stress that confers atopy risk, as well as the potentially modifiable protective factors that may attenuate this relationship.

A relationship between prenatal maternal stress and offspring atopic diseases has been established yet remains poorly understood (Marshall, 2014). Stressful experiences early in development appear particularly important, with atopy risk beginning *in utero* and the developing immune and neuroendocrine systems remaining highly vulnerable throughout the first two years of life (Rosa et al., 2018). It is thought that a mother's own dysregulated stress response can result in a dysregulated fetal stress response, which may predispose offspring for atopy (for review, see Rosa et al., 2018). For instance, exposure to stress may induce alterations in a mother's hypothalamic-pituitary-adrenal (HPA) axis and immune system; a fetus reared in this prenatal environment may in turn develop altered HPA axis and immune functioning, engendering the development of atopy. In other words, a mother's own stress may become biologically embedded, not only disrupting her own physiological systems but also influencing health outcomes of her offspring (Rosa et al., 2018). Notably, "stress" is a multidimensional concept that can generally be thought of as objective environmental exposures (e.g., life events) or subjective responses (e.g., psychological perceptions; Harkness & Monroe, 2016). The most recent meta-analysis between prenatal maternal stress and offspring atopic diseases demonstrated the largest effects for psychological perceptions of stress, including anxiety and depression (Flanigan et al., 2018).

Although this work has been critical in establishing a link between maternal stress and offspring atopy, recent evidence suggests a need to examine maternal stress occurring even earlier than the prenatal period. For example, a recent study documented associations between maternal history of child abuse and offspring atopy at two years of age (Tomfohr-Madsen et al., 2016), controlling for socioeconomic status, sex, race, and preterm birth. Further analyses revealed this relationship was mediated by maternal anxiety and depressive symptoms in

pregnancy. This study highlights the importance of broadening our conceptualization of the prenatal stress-atopy connection to include stress during sensitive periods earlier in a mother's life, including her childhood. However, it was conducted in a predominately White, highly educated sample with a low prevalence of abuse; researchers called for future studies to consider whether these findings hold in more racially and socioeconomically diverse samples (Tomfohr-Madsen et al., 2016). A separate longitudinal study in a more diverse sample found that chronic maternal interpersonal trauma (IPT) was associated with increased cord blood Immunoglobulin E (IgE) levels (Sternthal et al., 2009) and asthma in male offspring during early childhood (Brunst et al., 2017), suggesting that maternal stress and child atopy associations are generalizable across diverse backgrounds. Notably, a broader conceptualization of stress may be particularly important in Black communities, which have experienced historical trauma and are continually exposed to racism across individual, institutional, and cultural levels (Bernard et al., 2020).

Although empirical evidence supports the association between maternal trauma across the lifespan and offspring atopic diseases, several methodological gaps remain. First, the extent to which maternal early life stress confers risk, compared to risk from maternal stress experienced during the more commonly studied prenatal period, remains unknown. Second, no previous studies were designed specifically to focus on the experience of Black Americans, who experience the highest rates of several types of stress, as well as atopy (Jones et al., 2019). Third, previous studies have been limited to self-report measures of stress, despite evidence that disrupted maternal stress physiology is associated with offspring atopy (Wright et al., 2013). In light of this, the current study used both self-report and physiological measures of stress.

Although maternal stress exposure may increase risk for atopy, not all children who are exposed to maternal stress go on to develop atopic diseases. To prevent atopic diseases from developing, and to intervene when they do, it is important to identify modifiable factors that may increase or decrease the strength of the maternal stress-child atopy relationship. Given that the primary caregiver exerts a profound influence on the extent to which early adversity sculpts a child's developing stress systems (Engel & Gunnar, 2020), sensitive and responsive caregiving by a mother may protect a child from many of the toxic effects of early stress exposure, including atopy. For instance, studies have found that maternal sensitivity protects against offspring atopic dermatitis in the context of perinatal anxiety (Letourneau et al., 2017) and that supportive caregiving buffers the effects of exposure to intimate partner violence on offspring asthma risk (Suglia et al., 2018). To date, no known study has examined the protective role of maternal warmth and responsiveness on offspring atopy using a life course perspective (i.e., broadening the conceptualization of maternal stress beyond the perinatal period), nor done so in a sample of Black American mother-child dyads.

In the current study, we will examine the intergenerational transmission of maternal stress and offspring risk for physician diagnosis of any atopic disease by two-to-three years of age in a cohort of 179 Black mother-child dyads, a group disproportionately affected by both maternal stress and atopic diseases yet vastly underrepresented in the empirical literature on these topics (Jones et al., 2019). First, we will examine whether different types of maternal stress increase atopy risk in offspring. We predict that maternal reports of childhood trauma, prenatal psychological stress (a composite of perceived stress, anxiety, and depression), and postnatal psychological stress will each increase risk for physician-diagnosis of offspring atopy. Likewise, we predict that physiological indicators of chronic maternal stress will also be associated with

increased atopy risk. Next, we will explore the protective role of maternal sensitivity on the relationship between maternal stress and offspring atopy. We predict that mother-infant interactions characterized by high maternal warmth and responsiveness will decrease the association between maternal stress and offspring atopy.

Methods

Participants and Procedure

Participants included 179 Black mother-child dyads recruited from an ongoing prospective longitudinal cohort study designed to examine the roots of child health disparities (Corwin et al., 2017). For this larger study, women were recruited between eight and 14 weeks of pregnancy from two Atlanta metropolitan hospitals. One of these hospitals was private and one was public, resulting in a socioeconomically diverse sample. Following informed consent and participation in the prenatal study, women who had live births and whose infants were free of major congenital disorders were invited to enroll in a follow-up study designed to examine prenatal and early life exposures in relation to child health outcomes, with annual follow-ups when the children were two and three years of age. Inclusion criteria for the current study include (1) participation in the prenatal and age two-to-three year studies, (2) maternal report of offspring health status at age two or three years, and (3) maternal self-reports of stress at one or more time points. A subset of these mothers and infants (n = 70) also participated in a study of infant development in which mother-child interaction patterns were assessed (Brennan et al., 2019); only these dyads were included in our examination of maternal warmth and responsivity.

During the first trimester of pregnancy, women provided demographic information, self-report of childhood trauma, and a blood sample for a white blood cell dexamethasone sensitivity assay. During the third trimester of pregnancy, women completed self-report measures of stress,

depression, and anxiety. When offspring were six, 12, and/or 18 months of age, mother-infant dyads completed a behavioral task to assess warm and responsive parenting. Finally, when offspring were two-to-three years of age, mothers completed self-report measures of stress, depression, and anxiety, as well as reports of any physician diagnosis of offspring atopy. All mothers provided informed consent for their own and their child's participation and all procedures were approved by the Emory University IRB.

Measures

Demographic and Prenatal and Neonatal Health Measures

Mothers provided information on a range of demographic and health factors. As part of the prenatal study, mothers reported their age in years, current tobacco use (yes/no), marital status, highest level of education, family income, and type of medical insurance. Maternal height and weight were also assessed to calculate maternal prenatal body mass index (BMI). In addition, information regarding child sex, birthweight, gestational age, and mode of delivery was extracted from neonatal medical records.

Maternal Atopy. As part of the early childhood follow-up, mothers reported whether they had been diagnosed by a health care professional with any of the following: (1) Asthma, (2) Eczema, (3) Hayfever, (4) Seasonal Allergy, and (5) Food Allergy. Maternal atopy was coded present or absent, with the endorsement of any one or more of these diagnoses indicating the presence of atopy.

Offspring Atopy. When offspring were two-to-three years of age, mothers were asked, "Has your child been diagnosed with any of the following? (1) Asthma, (2) Atopic Dermatitis or Eczema, (3) Seasonal or Pollen Allergies, (4) Food Allergy?" Offspring atopy was coded present or absent, such that endorsement of one or more of these diagnoses was considered present.

Maternal Stress

Childhood Trauma. Women retrospectively reported their childhood trauma using the short form of the Childhood Trauma Questionnaire (CTQ-SF; Bernstein et al., 2003), a 28-item self-report measure designed to assess a diverse array of traumatic childhood experiences. The CTQ total score combines all items from the Physical Abuse, Sexual Abuse, Emotional Abuse, Physical Neglect, and Emotional Neglect subscales. Responses range from 1, "never true," to 5, "very often true," such that higher scores indicate more severe abuse and neglect. In the current sample, $\alpha = .88$ for the total scale.

Prenatal Psychological Stress. Principal Component Analysis (PCA) using participant data from the prenatal study cohort (N = 485) suggested that maternal stress and demographic measures fell on separate dimensions of prenatal psychological stress and sociodemographic adversity. On the basis of this PCA, maternal prenatal psychological stress was operationalized as a composite of three self-report measures completed during the third trimester of pregnancy. Each separate scale was standardized, and the average of the standardized scores was used in all analyses. Specifically, our prenatal psychological stress measure reflects (1) perceived stress, (2) anxiety symptoms, and (3) depressive symptoms.

Perceived Stress. Maternal perceived stress was assessed with the Perceived Stress Scale (PSS; Cohen, 1988). This 10-item measure is designed to gauge how overloaded, uncontrollable, or unpredictable individuals perceive their current lives to be. Responses range from 0, "Never," to 4, "Very Often," with higher total scores indicating perceptions of greater stress. In the current sample, $\alpha = .69$.

Anxiety Symptoms. Maternal anxiety symptoms were assessed with the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983), a 40-item measure of state and trait anxiety. This

study used the 20-item S-anxiety scale, which exclusively taps into state anxiety, or how anxious individuals feel in the moment. Responses range from 1, “Not at all,” to 4, “Very much so,” with higher total scores indicating greater symptoms of anxiety. In the current sample, $\alpha = .92$.

Depressive Symptoms. Maternal depressive symptoms were assessed with the Edinburgh Postnatal Depression Scale (EPDS; Cox et al., 2003), a 10-item questionnaire used to screen women for depressive symptoms during and following pregnancy. Participants indicate to what extent each symptom describes them, with responses ranging from zero to three and higher total scores indicating greater symptoms of depression. In the current sample, $\alpha = .89$.

Postnatal Psychological Stress. Each of the three above measures (PSS, STAI, EPDS) were repeated when offspring were two-to-three years of age to assess postnatal psychological stress. Similar to the prenatal measures, these three scales were combined to create a composite variable representing maternal postnatal psychological stress. For the PSS, $\alpha = .77$ at offspring age two and .76 at offspring age three. For the STAI, $\alpha = .92$ at offspring age two and .90 at offspring age three. For the EPDS, $\alpha = .83$ at offspring age two and .73 at offspring age three.

Physiological Indicators of Chronic Stress Exposure. The current study used absolute number of monocytes, obtained from a complete blood count, as well as two measures from the white blood cell dexamethasone sensitivity (DEX) test as previously described (Clarke et al., 2020; Corwin et al., 2017). The first measure, maximum Tumor Necrosis Alpha (TNFα) response, assessed the degree to which white blood cells mount an inflammatory response in the absence of glucocorticoids, when stimulated in vitro with lipopolysaccharide (LPS), or bacterial endotoxin. The second measure, DEX IC_{50}, assessed the concentration of dexamethasone needed to suppress 50% of the TNFα response. In other words, the TNFα response reflects the inflammatory response produced when exposed to infectious stimuli, whereas DEX IC_{50} reflects

glucocorticoid resistance. Higher values of TNFα indicate greater inflammatory propensity while higher values of DEX IC_{50} indicate greater resistance to the anti-inflammatory signals of glucocorticoids, commonly referred to as 'glucocorticoid resistance'. Glucocorticoid resistance was identified over thirty years ago (Chrousos, 1995) as an indicator of chronic stress exposure. In this study, we hypothesized that higher values of both of these measures would predict offspring atopy. These hypotheses were based on literature linking chronic stress to both elevated production of proinflammatory cytokines (Coussons-Read et al., 2007) and elevated glucocorticoid resistance (Corwin et al., 2020) in prenatal women.

Warm and Responsive Parenting

When infants were six, 12, and 18-months of age, mother-infant dyads were videotaped during a five-minute play interaction, which was rated offline using an adapted version of the Three-Bag Assessment (Brady-Smith et al., 2013). Mothers were provided with age-appropriate toys and instructed to play with their infants as they typically would. To enhance ecological validity, the majority of observations were conducted in the home setting (rather than in the lab), and experimenters left the room during the interaction. The assessment and coding scheme was adapted from the NICHD Study of Early Child Care and has been shown to demonstrate similar psychometric properties across African American, European American, and Latin American dyads in Early Head Start (Fuligni & Brooks-Gunn, 2013). Sensitivity was operationalized as a mother's ability to cultivate a child-centered interaction, which involves high responsiveness to the infant's affect and interests, encouragement, and praise. Positive Regard was operationalized as a mother's observed warmth towards and enjoyment of the infant, and includes positive facial expressions, warm vocal tone, and displays of physical affection. Ratings for each variable fall on a scale ranging from one to four points, where one suggests little to no evidence of the

variable, and four represents the highest demonstration of said variable. Raters were blind to family socioeconomic status, maternal stress, and maternal and offspring atopy. A reliability analysis on 20% of all rated data yielded intra class correlations of 0.88 or greater. Given high correlations between Sensitivity and Positive Regard (*r's* = .46-.79, *p's* < 0.001), we summed these variables to create a "Warm and Responsive Parenting" index, with scores ranging from two to eight.

Data Analytic Plan

All analyses were conducted using IBM SPSS Statistics, version 26 (Armonk, NY, USA). For the physiological stress measures, outliers greater than three standard deviations from the mean were removed. For TNFα response, the natural log was taken to reduce skewness and kurtosis. For composite measures, missing data was replaced with the mean of the available items. To maximize sample size, data from two- and three-year postnatal visits were combined. If participants came at only one time point, that data was used. If they came at both time points, maternal stress measures were averaged, and offspring atopy reported at either time point was coded as present. To maximize sample size for the mother-child interaction task, scores across the six, 12, and 18 month visits were averaged.

Independent-samples *t* tests for continuous variables and χ^2 tests for categorical variables were performed to identify whether offspring atopy was associated with a variety of potential demographic and health covariates. Logistic regression was performed to examine whether each measure of maternal stress was associated with offspring atopy after adjusting for significant covariates. For the biological stress analyses, maternal BMI and number of monocytes were selected as covariates a priori, as is standard practice when examining DEX sensitivity. For analyses examining parenting as a moderator, warm and responsive parenting was first mean-

centered. Power analyses conducted using G*Power 3.1 (Faul et al., 2009) indicated that our sample was sufficiently powered to detect a small effect of the relationship between each maternal stress measure and offspring atopy.

Results

Demographic and descriptive characteristics of our sample are presented in Table 1. In further support of combining the self-reported stress measures into a composite psychological stress variable, maternal PSS, STAI, and EPDS scores were highly correlated (prenatal: *r*'s = .66-.71, *p*'s < .001; postnatal: *r*'s = .65-.74, *p*'s < .001). Maternal report of childhood trauma was significantly correlated with prenatal ($r = .34$, $p < .001$) and postnatal psychological stress ($r = .34$, $p < .001$); maternal reports of prenatal and postnatal psychological stress were also significantly correlated with one another ($r = .51$, $p < .001$). Similarly, maximum TNFα response and DEX IC_{50} measures were significantly correlated with one another ($r =. 16$, $p = .046$). Notably, maternal self-report and physiological stress measures were uncorrelated. Covariate analyses revealed that offspring atopy was significantly associated with offspring sex ($\chi^2 = 4.27$, $p = .039$), such that males were more likely to have atopy than were females, and maternal atopy ($\chi^2 = 7.17$, $p = .007$), such that mothers with a history of atopy were more likely to have an offspring with atopy. None of the other tested covariates, including SES index, maternal age, maternal BMI, prenatal tobacco exposure, mode of delivery, birthweight, or length of breastfeeding were significantly associated with offspring atopy. All logistic regressions included offspring sex and maternal atopy as covariates.

Results of all logistic regression analyses are presented in Table 2. In contrast to our hypotheses, none of the self-reported maternal stress variables were associated with offspring atopy at two-to-three years of age. DEX IC_{50}, or the degree of maternal glucocorticoid resistance,

was also not associated with offspring atopy. Unexpectedly, maternal maximum TNFα response was *negatively* associated with offspring atopy, such that mothers who produced a smaller inflammatory response were more likely to have an offspring with an atopic disease (β = -.65, *Wald* = 6.69, *p* = .01).

Parenting did not emerge as a significant moderator in the relationship between maternal childhood trauma, DEX IC_{50}, or TNFα response and offspring atopy. However, it is notable that warm and responsive parenting significantly interacted with both maternal prenatal and postnatal psychological stress in predicting offspring atopy (Table 2). We used SPSS PROCESS (version 3.5) to confirm significant interaction effects with bootstrap sampling and to examine the pattern and direction of the interaction. The interaction effect of maternal prenatal psychological stress and warm and responsive parenting was significant (Z = -2.42, *p* = .02, β = -.80 CI =-1.45, -.15). As hypothesized, warm and responsive parenting demonstrated a protective effect. Prenatal stress only predicted increased risk for child atopy when the levels of warm and responsive parenting were low (Z = 2.01, *p* = .04, β = 2.43, CI = .06, 4.80). A similar pattern was evident for the interaction of maternal postnatal psychological stress and warm and responsive parenting (Z = -2.88, *p* = .004, β = -.72, CI = -1.20, -.23), with postnatal stress only predicting increased risk for child atopy when the levels of warm and responsive parenting were low (Z = 2.24, *p* = .03, β = 1.78, CI = .23, 3.33).

Discussion

This study aligns with recent calls in the *Journal of Pediatric Psychology* to move beyond detecting health disparities and towards understanding their underlying mechanisms (e.g., Valrie et al., 2020). Elucidating the factors underlying racial disparities in atopy prevalence is critical; only once these are understood can findings be translated into interventions and policy change to

reduce and/or eliminate such disparities (Kilbourne et al., 2006). In the only known investigation in an exclusively Black sample to examine maternal stress and offspring atopy across multiple levels of analysis, we found that the maternal stress-offspring atopy relationship may be more nuanced than results from recent meta-analyses have suggested. Findings from predominately White samples may not directly generalize to Black populations, and an expanded conceptualization of stress in Black Americans may be warranted.

Contrary to our expectations, we found no association between maternal reports of childhood trauma, prenatal psychological stress, or postnatal psychological stress and offspring atopy. These null findings are unexpected; accumulating epidemiological studies, meta-analyses, and reviews have highlighted the relationship between maternal self-reported stress and offspring atopy. However, a closer examination of individual studies reveals heterogeneity in terms of type and timing of stress, as well as atopy outcome. While previous work has largely examined different self-report measures of stress separately, we chose to conceptualize maternal prenatal and postnatal psychological stress more broadly based on both theory and the underlying factor structure of these constructs. It is important to note that our measures of prenatal and postnatal psychological stress were all self-reported perceptions, whereas several studies have assessed stress via more objective reports of negative life events (Wright et al., 2010).

Critically, our dissimilar findings from previous research also raise questions about this field's heavy reliance on White samples of high socioeconomic status. Of the 31 studies analyzed in Flanigan et al. (2018), only six studies included Black Americans, with only two samples reporting above 30% inclusion. A growing body of research suggests a possibility of measurement invariance, whereby self-reported perinatal stress measures may not reflect or be predictive of the same constructs across cultures (NRC, 2004). For instance, while several

studies have reported prenatal psychosocial stress as a risk factor for preterm birth, a recent study of Puerto Rican women employed validated measures of negative life events, perceived stress, depression, and neighborhood perceptions and identified no associations with preterm birth (Eick et al., 2020). As others have suggested, our current measures of stress do not reflect the unique stressors of Black Americans, such as historical trauma, chronic racial discrimination, and systemic racism (Bernard et al., 2020). Recently, a Culturally-Informed Adverse Childhood Experiences framework (C-ACE) has been proposed, which emphasizes the traumatic and enduring biopsychosocial effects of racism on health outcomes across generations (Bernard et al., 2020). We encourage future researchers to follow this framework, striving to capture the historical trauma (e.g., moving beyond a mother's experiences of trauma and focusing on longstanding patterns of injustice), social conditions (e.g., access to medical care, neighborhood violence), and racism across several levels (e.g., individual discrimination, institutional policies, cultural stereotypes) experienced by Black Americans.

Our overarching hypothesis was that maternal exposure to psychological stress would result in alterations in stress-mediating physiological systems, and that offspring reared in a prenatal environment characterized by such physiological alterations would evince heightened risk for stress and immune-mediated health outcomes, including atopic diseases. Our results provide partial support for this hypothesis, particularly in regard to one of our physiological measures. Maternal inflammatory cytokine release in response to stimulation was prospectively associated with offspring atopy, even after controlling for offspring sex, number of monocytes, maternal BMI, and maternal atopy history. The direction of this association may be surprising if one expects women producing greater inflammatory responses to be more likely to have offspring with atopic diseases. However, the literature examining psychological stress and TNFα

production is quite mixed (Huang et al., 2011; Steptoe et al., 2007), and our findings parallel a study that found lower TNFα production in PTSD patients relative to healthy controls (De Kloet et al., 2007). In addition, our inflammatory cytokine measured was TNFα, a T-helper 1 (Th1) cytokine. Atopy is characterized by a Th2 cytokine profile, in which the immune system is skewed towards a smaller proportion of Th1 relative to Th2 cytokines (Karlsson et al., 2017). Thus, the current finding suggests these women who released smaller amounts of TNFα may have a Th2 profile, which may program offspring for atopy *in utero*. A limited number of human studies have linked prenatal maternal psychological stress to increased Th2 and decreased Th1 responses to immune stimulation (Al-Hussainy & Mohammed, 2020). Furthermore, one study prospectively identified that women with a stronger Th2 profile during the first trimester, characterized by decreased TNFα levels, were more likely to have offspring who went on to develop offspring wheeze and allergic disease at three years of age (Kim et al., 2008). Our current findings replicate this work.

While our three psychological measures of stress were significantly correlated, as were our two physiological measures, our psychological and physiological measures were not related. Our results may reflect differences between psychological and physiological measures of stress, in line with other work suggesting that physiological measures may better capture prenatal stress in Black women than the self-report measures currently available. For instance, one study of predominately Black women found that while perceived stress did not predict preterm birth, prenatal cortisol levels did (Masho & Price, 2015). Alternatively, our results may reflect the chronicity of stress. As other researchers have noted, chronic stress is very difficult to capture through self-reports (Harkness & Monroe, 2016). While we employed measures of stress at three time points—childhood, prenatal, early postnatal—we did not capture the majority of

adolescence and adulthood. Our significant physiological finding may reflect immune alterations induced by chronic stress exposure. Developing comprehensive lifespan measures of stress-- and measures that reflect the systemic stressors faced by Black Americans in particular-- is an important direction for future research.

Although our findings were on a subsample, suggesting a need for replication, we did note preliminary evidence for a potentially protective role of warm and responsive parenting in the relationships between both prenatal and postnatal stress and offspring atopy. In the context of self-reported prenatal and postnatal maternal stress, mothers who demonstrated sensitive caregiving and positive regard were less likely to have offspring who developed atopy. Previous evidence supporting this relationship has been limited to relatively affluent White populations (e.g., Letourneau et al., 2017); thus, our study expands the literature as the first known investigation to suggest these effects may translate to Black populations as well. Our preliminary findings offer hope in that parenting is readily modifiable (EPIC, 2019), and we encourage future studies to explore the protective role of parenting in larger longitudinal samples.

This study has several limitations that we must acknowledge. Perhaps most striking, the small sample size in our analyses examining parenting as a moderator reflects low power to detect interaction effects. While this finding must be taken with caution, we feel it is promising and encourage future research to examine this malleable protective factor. Although our parenting measure was limited to a five-minute videotaped interaction, observational methods have been superior to maternal reports of parenting in predicting child outcomes in low-income families (Zaslow et al., 2006). Our study is also limited to maternal self-reports of physician-diagnoses of both maternal and offspring atopy at two-to-three years of age. That being said, previous studies have suggested that maternal reports of diagnoses are generally valid (Hansen et

al., 2015), and the peak age of diagnosis of each of these conditions was within our age range (0-5 months, 12-17 months, 24-29 months, 12-17 months for eczema, asthma, allergic rhinitis, food allergy, respectively; Hill et al., 2016). Though traditionally noted as a limitation, previous research has indeed relied on maternal reports of diagnoses in young ages (e.g., Tomfohr-Madsen et al., 2016). While our dichotomous measure of atopy can be seen as a limitation, we also feel it is a strength. The classic "atopic march" theory describes the onset of eczema and food allergy in infancy followed by asthma and allergic rhinitis in childhood, yet this temporal pattern is far from universal (Yang et al., 2020). Thus, our approach captures the greatest number of children at risk for atopy morbidity. Turning to stress, we were limited by the inherent difficulty of capturing chronic stress (Harkness & Monroe, 2016). Although our physiological measures of stress, in theory, capture stress across the lifespan, our self-report questionnaires captured stress at distinct time points. Even if we had created a chronic stress measure with these three variables, it would have failed to capture several years of life. Furthermore, though widely used, our self-reported measures reflect universal constructs rather than the chronic discrimination and systemic racism unique to Black Americans. These limitations withstanding, we feel our study had many notable strengths, including a prospective, longitudinal design; lifespan perspective; and consideration of several relevant covariates. We included measures across multiple levels of analysis, including self-reported perceptions of psychological stress, behavioral observations, and physiological assessments. Most importantly, this research was conducted in a sample that is at highest risk for both stress and atopy yet sorely understudied (Jones et al., 2019).

In the first known study to multidimensionally examine the relationship between maternal stress and offspring atopy in Black mother-child dyads, we noted dissimilar relationships

compared to what has previously been found in White samples. We found that a physiological marker of maternal stress in pregnancy prospectively predicted offspring atopy in the opposite direction as predicted. While our findings are largely null, we do not want to convey that stress is not an important contributor to the profound health disparities surrounding atopic diseases. Rather, we believe the relationship may be more nuanced, and we encourage future studies to further examine the systemic stressors experienced by Black Americans, perhaps beginning with ethnography, focus groups, or other qualitative methods and progressing towards measures that more collectively capture the stress specific to Black women. A culturally valid conceptualization of maternal stress is essential to assessing its role in atopy and other morbidity and mortality among Black children. Furthermore, we identified warm and responsive parenting as a potential protective factor, which may inform future intervention research. Overall, our findings underscore the importance of diversity, inclusion, and equity in behavioral health research, and we encourage replication in larger studies of Black women and children.

References

Al-Hussainy, A., & Mohammed, R. (2020). Consequences of maternal psychological stress during pregnancy for the risk of asthma in the offspring. *Scandinavian Journal of Immunology*, *January*, 1–13.

Bernard, D. L., Calhoun, C. D., Banks, D. E., Halliday, C. A., Hughes-Halbert, C., & Danielson, C. K. (2020). Making the "C-ACE" for a Culturally-Informed Adverse Childhood Experiences Framework to Understand the Pervasive Mental Health Impact of Racism on Black Youth. *Journal of Child and Adolescent Trauma*.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse and Neglect*, *27*(2), 169–190.

Brady-Smith, C., Brooks-Gunn, J., Tamis-LeMonda, C. S., Ispa, J. M., Fuligni, A. S., Chazan-Cohen, R., & Fine, M. A. (2013). Mother-Infant Interactions in Early Head Start: A Person-Oriented Within-Ethnic Group Approach. *Parenting*, *13*(1), 27–43.

Brennan, P. A., Dunlop, A. L., Smith, A. K., Kramer, M., Mulle, J., & Corwin, E. J. (2019). Protocol for the Emory University African American maternal stress and infant gut microbiome cohort study. *BMC Pediatrics*, *19*(1), 1–9.

Brunst, K. J., Rosa, M. J., Jara, C., Lipton, L. R., Lee, A., Coull, B. A., & Wright, R. J. (2017). Impact of Maternal Lifetime Interpersonal Trauma on Children's Asthma: Mediation Through Maternal Active Asthma during Pregnancy. *Psychosom. Med.*, *79*(1), 91–100.

Centers for Disease Control and Prevention (2018). *Most recent national asthma data.* https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm

Chen Arroyo, A. (2017, March 7). *Where do children with asthma die? A national perspective from 2003 to 2014.* [Conference presentation]. 2017 American Academy of Allergy, Asthma & Immunology Annual Meeting, Atlanta, GA, United States.

Chorousos, G. (1995). The hypothalamic-pituitary-adrenal axis and immune-mediated inflammation. *New England Journal of Medicine, 332*(20), 1351-1363.

Clarke, L. S., Corwin, E. J., Dunlop, A. L., Hankus, A., Bradner, J. M., Paul, S., Jiao, Y., Smith, A. K., Patrushev, N., Mulle, J. G., Read, T. D., Hogue, C. J. R., & Pearce, B. D. (2020). Glucocorticoid receptor sensitivity in early pregnancy in an African American cohort. In *American Journal of Reproductive Immunology* (Vol. 84, Issue 1).

Cohen, S. (1988). *Perceived stress in a probability sample of the United States.* In S. Spacapan & S. Oskamp (Eds.), *The Claremont Symposium on Applied Social Psychology. The social psychology of health* (p. 31–67). Sage Publications, Inc.

Corwin, E., Dunlop, A. L., Fernandes, J., Li, S., Pearce, B., & Jones, D.P. (2020). Metabolites and metabolic pathways associated with glucocorticoid resistance in pregnant African-American women. *Comprehensive Psychoneuroendocrinology, 1.*

Corwin, E. J., Hogue, C. J., Pearce, B., Hill, C. C., Read, T. D., Mulle, J., & Dunlop, A. L. (2017). Protocol for the Emory University African American Vaginal, Oral, and Gut Microbiome in Pregnancy Cohort Study. *BMC Pregnancy and Childbirth, 17*(1), 1–8.

Coussons-Read, M. E., Okun, M. L., & Nettles, C. D. (2007). Psychosocial stress increases inflammatory markers and alters cytokine production across pregnancy. *Brain, Behavior, & Immunity, 21*(3), 343-350.

Cox, J., & Holden, J. (2003). *Perinatal mental health: A guide to the Edinburgh Postnatal Depression Scale (EPDS).* Royal College of Psychiatrists.

Daya, M., & Barnes, K. C. (2019). African American ancestry contribution to asthma and atopic dermatitis. *Annals of Allergy, Asthma and Immunology*, *122*(5), 456–462.

De Kloet, C. S., Vermetten, E., Bikker, A., Meulman, E., Geuze, E., Kavelaars, A., Westenberg, H. G. M., & Heijnen, C. J. (2007). Leukocyte glucocorticoid receptor expression and immunoregulation in veterans with and without post-traumatic stress disorder. *Molecular Psychiatry*, *12*(5), 443–453.

Eick, S. M., Meeker, J. D., Swartzendruber, A., Rios-McConnell, R., Brown, P., Vélez-Vega, C., Shen, Y., Alshawabkeh, A. N., Cordero, J. F., & Ferguson, K. K. (2020). Relationships between psychosocial factors during pregnancy and preterm birth in Puerto Rico. *PLoS ONE*, *15*(1), 1–14.

Engel, M.L., & Gunnar, M.R. (2020). The development of the human hypothalamic-pituitary-adrenocortical axis: Sensitive periods and regulatory processes. In A. Clow, & N. Smyth (Eds.), *International review of neurobiology: Stress and brain health: across the life course* (Vol. 150). Academic Press.

European Platform for Investing in Children (2019). *Positive parenting interventions: Empowering parents with positive parenting techniques for lifelong health and well-being.* https://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=8209&furtherPubs=yes&fbclid=IwAR2AN1MCfMOymNsmTx_18f4mleyTrY9RAZDwLbV6HuBypVeK-n2hegFS0V8

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*, 1149-1160.

Flanigan, C., Sheikh, A., DunnGalvin, A., Brew, B. K., Almqvist, C., & Nwaru, B. I. (2018). Prenatal maternal psychosocial stress and offspring's asthma and allergic disease: A systematic review and meta-analysis. In *Clinical and Experimental Allergy* (Vol. 48, Issue 4, pp. 403–414).

Fuligni, A. S., & Brooks-Gunn, J. (2013). Mother Child Interactions in Early Head Start Age and Ethnic Differences in Low Income Dyads. *Parenting: Science and Practice*, *13*(1), 1–26.

Halken, S. (2004). Prevention of allergic disease in childhood: Clinical and epidemiological aspects of primary and secondary allergy prevention. *Pediatric Allergy and Immunology, Supplement*, *15*(16), 9–32.

Hansen, T. E., Evjenth, B., & Holt, J. (2015). Validation of a questionnaire against clinical assessment in the diagnosis of asthma in school children. *J Asthma*, *52*(3), 262–7.

Harkness, K. L., & Monroe, S. M. (2016). The assessment and measurement of adult life stress: Basic premises, operational principles, and design requirements. *Journal of Abnormal Psychology*, *125*(5), 727–745.

Hill, D. A., Grundmeier, R. W., Ram, G., & Spergel, J. M. (2016). The epidemiologic characteristics of healthcare provider-diagnosed eczema, asthma, allergic rhinitis, and food allergy in children: A retrospective cohort study. *BMC Pediatrics*, *16*(1), 1–8.

Huang, C. J., Stewart, J. K., Franco, R. L., Evans, R. K., Lee, Z. P., Cruz, T. D., Webb, H. E., & Acevedo, E. O. (2011). LPS-stimulated tumor necrosis factor-alpha and interleukin-6 mRNA and cytokine responses following acute psychological stress. *Psychoneuroendocrinology*, *36*(10), 1553–1561.

Jones, B. L., Staggs, V., & Woods-Jaeger, B. (2019). Chronic stress exposure among young African American children with asthma: Racism is a factor. *Annals of Allergy, Asthma and*

Immunology, *123*(5), 507–508.

Karlsson, L., Nousiainen, N., Scheinin, N. M., Maksimow, M., Salmi, M., Lehto, S. M., Tolvanen, M., Lukkarinen, H., & Karlsson, H. (2017). Cytokine profile and maternal depression and anxiety symptoms in mid-pregnancy—the FinnBrain Birth Cohort Study. *Archives of Women's Mental Health*, *20*(1), 39–48.

Keet, C. A., Savage, J. H., Seopaul, S., Peng, R. D., Wood, R. A., & Matsui, E. C. (2014). Temporal trends and racial/ethnic disparity in self-reported food allergy in the United States. *Ann Allergy Asthma Immunol.*, *112*(3), 222-229.

Kilbourne, A. M., Switzer, G., Hyman, K., Crowley-Matoka, M., & Fine, M. J. (2006). Advancing health disparities research within the health care system: A conceptual framework. *American Journal of Public Health*, *96*(12), 2113–2121.

Kim, J. H., Kim, K. H., Woo, H. Y., & Shim, J. Y. (2008). Maternal cytokine production during pregnancy and the development of childhood wheezing and allergic disease in offspring three years of age. *Journal of Asthma*, *45*(10), 948–952.

Kim, Y., Blomberg, M., Rifas-Shiman, S. L., Camargo, C. A., Gold, D. R., Thyssen, J. P., Litonjua, A. A., Oken, E., & Asgari, M. M. (2019). Racial/Ethnic Differences in Incidence and Persistence of Childhood Atopic Dermatitis. *Journal of Investigative Dermatology*, *139*(4), 827–834.

Letourneau, N. L., Kozyrskyj, A. L., Cosic, N., Ntanda, H. N., Anis, L., Hart, M. J., Campbell, T. S., & Giesbrecht, G. F. (2017). Maternal sensitivity and social support protect against childhood atopic dermatitis. *Allergy, Asthma and Clinical Immunology*, *13*(1), 1–14.

Marshall, G. D. (2014). Stress and allergic diseases - Still under recognized and undertreated. *Annals of Allergy, Asthma and Immunology*, *112*(4), 275.

Masho, S., & Price, S. (2015). Racial Disparities in the Association Between Stress and Preterm Birth. *Journal of Health Disparities Research and Practice*, *8*(4), 80–92.

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological Stress in Childhood and Susceptibility to the Chronic Diseases of Aging: Moving Towards a Model of Behavioral and Biological Mechanisms. *Psychol Bull*, *137*(6), 959–997.

National Research Council (2004). Understanding racial and ethnic differences in health in late life: A research agenda. Washington, DC: The National Academies Press.

Rosa, M. J., Lee, A. G., & Wright, R. J. (2018). Evidence establishing a link between prenatal and early-life stress and asthma development. *Current Opinion in Allergy and Clinical Immunology*, *18*(2), 148–158.

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.

Steptoe, A., Hamer, M., & Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: A review and meta-analysis. *Brain, Behavior, and Immunity*, *21*(7), 901–912.

Sternthal, M. J., Enlow, M. B., Cohen, S., Canner, M. J., Staudenmayer, J., Tsang, K., & Wright, R. J. (2009). Maternal interpersonal trauma and cord blood IgE levels in an inner-city cohort: A life-course perspective. *J Allergy Clin Immun*, *124*(5), 954–960.

Suglia, S. F., Koenen, K. C., Boynton-Jarrett, R., Chan, P. S., Clark, C. J., Danese, A., Faith, M. S., Goldstein, B. I., Hayman, L. L., Isasi, C. R., Pratt, C. A., Slopen, N., Sumner, J. A., Turer, A., Turer, C. B., & Zachariah, J. P. (2018). Childhood and Adolescent Adversity and Cardiometabolic Outcomes: A Scientific Statement from the American Heart Association. *Circulation*, *137*(5), e15–e28.

Tomfohr-Madsen, L. M., Bayrampour, H., & Tough, S. (2016). Maternal history of childhood abuse and risk of asthma and allergy in 2-year-old children. *Psychosomatic Medicine*, *78*(9), 1031–1042.

Valrie, C., Thurston, I., & Santos, M. (2020). Introduction to the Special Issue: Addressing Health Disparities in Pediatric Psychology. *J Pediatr Psychol*, *45*(8), 833–838.

Wegienka, G., Havstad, S., Joseph, C. L. M., Zoratti, E., Ownby, D., Woodcroft, K., & Johnson, C. C. (2012). Racial Disparities in Allergic Outcomes in African Americans Emerge as Early as Age 2 Years. *Clin Exp Allergy*, *42*(6), 909–917.

Wright, R. J., Fisher, K., Chiu, Y.-H. M., Wright, R. O., Fein, R., Cohen, S., & Coull, B. A. (2013). Disrupted Prenatal Maternal Cortisol, Maternal Obesity, and Childhood Wheeze: Insights into Prenatal Programming. *Am J Respir Crit Care Med*, *187*(11), 1186–1193.

Wright, R. J., Visness, C. M., Calatroni, A., Grayson, M. H., Gold, D. R., Sandel, M. T., Lee-Parritz, A., Wood, R. A., Kattan, M., Bloomberg, G. R., Burger, M., Togias, A., Witter, F. R., Sperling, R. S., Sadovsky, Y., & Gern, J. E. (2010). Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner-city cohort. *American Journal of Respiratory and Critical Care Medicine*, *182*(1), 25–33.

Yang, L., Fu, J., & Zhou, Y. (2020). Research Progress in Atopic March. *Frontiers in Immunology*, *11*(August), 1–11.

Zaslow, M. J., Weinfield, N. S., Gallagher, M., Hair, E. C., Ogawa, J. R., Egeland, B., ... & De Temple, J. M. (2006). Longitudinal prediction of child outcomes from differing measures of parenting in a low-income sample. *Developmental Psychology*, *42*(1), 27.

Table 1

Demographic and Descriptive Characteristics

	N (%)	*M (SD)*
Demographic and Health Factors		
Offspring sex, female	90 (50.28)	
Maternal education		
</= 8th grade	1 (.60)	
Some high school	24 (13.40)	
Graduated high school/GED	70 (39.10)	
Some college/technical school	56 (31.30)	
Graduated college	21 (11.70)	
Some graduate work/degree	7 (3.90)	
Maternal health insurance		
Private	37 (20.67)	
Medicaid, Right from the Start[a]	69 (38.55)	
Medicaid, Low-Income	73 (40.78)	
Maternal tobacco exposure		
1st trimester, yes	23 (12.80)	
3rd trimester, yes	9 (5.00)	
Maternal atopy diagnosis, yes	56 (31.28)	
Maternal BMI, 1st trimester		29.16 (7.92)
Maternal prenatal absolute monocytes		.78 (3.48)
Mode of delivery, C-section	47 (26.26)	
Gestational age, weeks.days		38.60 (2.03)
Birthweight, kg		3.07 (0.54)
Breastfeeding length, weeks		4.10 (4.60)
Offspring Atopy, yes	67 (37.40)	
Asthma	24 (13.40)	
Eczema	40 (22.30)	
Seasonal allergies	17 (9.50)	
Food allergy	17 (9.50)	
Maternal Stress Measures		
Childhood trauma (CTQ)		41.56 (18.55)
Prenatal perceived stress (PSS)		23.52 (7.63)
Prenatal depression (EPDS)[b]		7.04 (6.04)
Prenatal anxiety (STAI)[c]		35.65 (11.65)
Postnatal perceived stress (PSS) age 2		20.66 (8.34)
Postnatal depression (EPDS) age 2		5.34 (4.57)
Postnatal anxiety (STAI) age 2		30.84 (10.38)
Postnatal perceived stress (PSS) age 3		20.95 (7.92)
Postnatal depression (EPDS) age 3		30.19 (9.38)
Postnatal anxiety (STAI) age 3		4.79 (3.61)
Maximum TNFα response, pgml		695.85 (448.36)
DEX IC_{50}, pmol		9978.08 (6552.16)
Warm and Responsive Parenting		5.92 (1.41)

Note: [a]Right from the Start (RSM) Medicaid is a type of Medicaid offered through the Georgia Department of Human Services. RSM provides medical care for pregnant women, including labor, delivery, and services for up to 60 days post-delivery. The ceiling for RSM eligibility is 200 percent of the federal poverty level; [b]Clinical cut score for the EPDS in minority women is 10; [c]Clinical cut score for the STAI is 40.

Table 2

Logistic Regression of Maternal Stress and Offspring Atopy at Ages 2-3

	N	*Wald*	*p*	*Exp (B)*	95% CI for *Exp (B)*	
					Lower	Upper
Childhood trauma	169	.039	.844	.998	.980	1.016
Prenatal psychological stress	168	1.916	.166	.765	.524	1.118
Postnatal psychological stress	176	.826	.363	.837	.570	1.229
Maximum TNFα response	**152**	**6.693**	**.010**	**.521**	**.318**	**.854**
DEX IC_{50}	150	.628	.428	1.00	1.000	1.000
Childhood trauma * warm and responsive parenting	68	.249	.618	1.005	.984	1.027
Prenatal psychological stress * warm and responsive parenting	**68**	**5.871**	**.015**	**.448**	**.234**	**.858**
Postnatal psychological stress * warm and responsive parenting	**69**	**8.279**	**.004**	**.489**	**.300**	**.796**
Maximum TNFα response * warm and responsive parenting	58	.052	.819	.925	.472	1.811
DEX IC_{50}* warm and responsive parenting	58	.325	.569	1.000	1.000	1.000

Note: Bolded values indicate significance, $p < .05$