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# Parental sensitivity modifies the associations between maternal prenatal stress exposure, autonomic nervous system functioning and infant temperament in a diverse, low-income sample

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**ABSTRACT**

Evidence suggests that adversity experienced during fetal development may shape infant physiologic functioning and temperament. Parental sensitivity is associated with child stress regulation and may act as a buffer against risk for intergenerational health effects of pre- or postnatal adversity. Building upon prior evidence in a racially and ethnically diverse sample of infants (M infant age = 6.5 months) and women of low socioeconomic status, this study examined whether coded parenting sensitivity moderated the association between an objective measure of prenatal stress exposures (Stressful Life Events (SLE)) and infant parasympathetic (respiratory sinus arrhythmia; RSA) or sympathetic (pre-ejection period; PEP) nervous system functioning assessed during administration of the Still-Face-Paradigm (SFP) ($n = 66$), as well as maternal report of temperament ($n = 154$). Results showed that parental sensitivity moderated the associations between prenatal stress exposures and infant RSA reactivity, RSA recovery, PEP recovery, and temperamental negativity. Findings indicate that greater parental sensitivity is associated with lower infant autonomic nervous system reactivity and greater recovery from challenge. Results support the hypothesis that parental sensitivity buffers infants from the risk of prenatal stress exposure associations with offspring cross-system physiologic reactivity and regulation, potentially shaping trajectories of health and development and promoting resilience.

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Prenatal programming; parenting; autonomic nervous system; temperament; DOHaD; stress

## 1. Introduction

Consistent with the developmental origins of health and disease (DOHaD) hypothesis, early adverse life experiences have been associated with a host of later negative health outcomes (Boyce, 2014; Shonkoff et al., 2009). One mechanism through which adverse

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experience may "get under the skin" to affect later health is by influencing the development of children's stress physiology and related emotional and behavioral regulation. This process appears to begin in utero (Arima & Fukuoka, 2020; Monk et al., 2019; Van den Bergh et al., 2017).

Prenatal stress is neither rare nor without consequence for offspring, particularly in low-SES or otherwise disadvantaged populations. Approximately 60–75% of pregnant women in the U.S. report at least one stressful life event during pregnancy (Mukherjee et al., 2017; USDHHS, 2013). Low-SES women report three or more prenatal stressful events (Ward et al., 2017). High levels of prenatal stress are associated with more negative health and behavioral outcomes in offspring, including temperament and stress reactivity (Van den Bergh et al., 2017), physical health issues (Entringer et al., 2015; Zijlmans et al., 2017) and alterations in brain structure and gut bacterium (Naude et al., 2020; Wu et al., 2020). Accumulating evidence, however, suggests that parenting may act as a programming agent of infant and child stress reactivity and recovery, and may act as a buffer against potential negative effects of adversity (Chen et al., 2011; Farrell et al., 2017; Gunnar, 2017). Although this body of research is growing, a greater understanding of these associations is needed in order to advance our understanding of the relationship between physiology and health, particularly in low-SES or non-privileged samples, and especially focused on the capacity of parenting to buffer the effects of stress.

This study builds upon reported findings from the Stress, Eating, and Early Development (SEED) study of racially/ethnically diverse, women with low socioeconomic status (SES) who reported experiencing a high degree of stress. In this under-studied population, Bush et al. (2017) showed that higher prenatal stress exposure, as assessed by the count of Stressful Life Events (SLE) (Centers for Disease Control and Prevention CDC, 2005; Senter et al., 2021), was associated with variations in maternal report of infant temperament, and with greater parasympathetic nervous system (PNS) reactivity to challenge and weaker PNS recovery in 6-month-old infants. Here, we extend that work to include examination of a measure of infant sympathetic nervous system (SNS) function, which is rarely included in infant developmental research, but, like the PNS, is a potential early life mechanism for health disparities. This study also advances the evidence by testing whether parenting sensitivity, assessed by trained raters using objective criteria, modifies the associations between prenatal stress exposure and infant autonomic nervous system (ANS) functioning or temperament, thus buffering the infant from the developmental risks associated with exposures to prenatal stress in utero.

Multiple biosocial models assert that offspring develop physiological and behavioral regulation within the context of the attachment relationship (Calkins & Hill, 2007; Cassidy, 1994). Parental sensitivity refers to the ability of the caregiver to recognize and accurately interpret infant signals and respond in a timely and appropriate manner (Ainsworth et al., 1978). Parental sensitivity is thought to be the mechanism by which parents help the infant regulate in the face of challenge and is associated with attachment security (Thompson et al., 2019). Thus, during times of infant distress, more sensitive parents enable infant self-regulation and help them avoid extensive periods of dysregulation (Perry et al., 2016; Sroufe, 1997). Children whose attachment figures do not respond, or respond inconsistently to their signals for help, may experience this as chronic stress, as they live in an environment with unpredictable safety and/or support. Both hyper and hypo-stress reactivity have been associated

with chronic stress exposure in childhood (NSCDC., 2005/2014; Struber et al., 2014). Particularly relevant to this study, extant research suggests that infant stress physiology activates during parental separation or disengagement but may recover at some point after reunion, particularly in samples from high-resource environments (Jones-Mason et al., 2018). Accordingly, in the attachment context, "buffering" refers to the association between the presence or availability of the attachment figure and the suppression or reduction of the child stress response in times of threat (Gunnar, 2017; Gunnar & Hostinar, 2015; Gunnar et al., 2015).

Because hyper or hypo-stress reactivity (a possible consequence of exposure to chronic stress) are each associated with negative long-term health outcomes including impaired cardiovascular, immune system, and endocrine functioning, the ability of the attachment relationship to promote a balanced infant physiological response to stressful challenge is of great interest (Gunnar & Vazquez, 2006; Jones-Mason et al., 2018). It is theorized that the buffering phenomenon may protect offspring from the association between threat exposures and health outcomes (Brown et al., 2020; Gunnar, 2017; Yirmiya et al., 2020). Accordingly, this study examined whether parenting sensitivity is associated with context-appropriate infant ANS reactivity and faster recovery from a standardized stressful challenge.

### *1.1. ANS: the parasympathetic and sympathetic nervous systems*

The ANS is part of the peripheral nervous system and facilitates individual adjustment to internal and external environmental changes, including responses to psychosocial stress (Mendes, 2009). The ANS has two major subdivisions: the parasympathetic (PNS) and sympathetic nervous (SNS) systems. Referred to as the "rest and digest system," the PNS acts to slow down bodily functions such as heart rate (HR), promote growth, and generally stimulate functions that occur when the body is resting such as digestion, elimination and salivation (Alkon et al., 2014). "Vagal tone," indexed by basal respiratory sinus arrhythmia (RSA), is thought to reflect resting PNS and acts as a significant indicator of self-regulatory capacity, particularly within the context of social interactions (Porges, 2007). Another PNS indicator, heart rate variability (HRV), refers to changes in time intervals between heartbeats (Shaffer & Ginsberg, 2017). RSA represents the variations in HR that occur with respiration (Zisner & Beauchaine, 2016), with higher RSA indicating greater PNS activity. Responsible for the "flight or fight" response, the SNS activates vigilance, arousal, and mobilization in response to perceived threats stimulating the heart to beat faster and the digestive system to slow down (Alkon et al., 2014). Thought to be a measure of "pure" SNS activity, pre-ejection period (PEP) represents the period from the electrical stimulation of the heart's left ventricle to the point at which the semilunar aortic valve opens and blood is ejected into the aorta (Cacioppo et al., 1994). PEP shortening reflects SNS activation. Extant research suggests that the ANS mediates the interaction between the infant and the environment (Porges, 2011). Accordingly, low resting RSA and chronic or excessive activation of RSA reactivity (abnormally low or large reductions in RSA during emotion elicitation (Beauchaine, 2015)) in children has been associated with poor emotion regulation including psychopathology such as anxiety, attention problems, conduct disorder, and externalizing or internalizing behaviors (Beauchaine, 2015; Hinnant & El-Sheikh, 2009). Higher resting RSA and lower RSA during challenge has been correlated with

positive emotions, social outcomes and effective regulation (Jones-Mason et al., 2018), although the literature is mixed (Eisenberg et al., 2012).

Far less research exists examining the association between SNS and outcomes in infants or in younger children and results within this developmental period are mixed. For example, one study reported that SNS activation is associated with higher externalizing or internalizing behaviors in kindergarten-aged children (Kalvin et al., 2016). Other studies, however, report that lower SNS activity at rest or in reaction to stressors may be associated with a higher risk for conduct problems, attentional problems, and reward insensitivity (e.g. Beauchaine et al., 2007, 2013; Crowell et al., 2006; Munoz & Anastassiou-Hadjicharalambous, 2011). A few studies have found higher skin conductance reactivity is associated with children's reactive aggression or externalizing behaviors (El-Sheikh, 2005; Hubbard et al., 2002) although others report that lower skin conductance reactivity is associated with child or adolescent externalizing problems (e.g. Fung et al., 2005; Snoek et al., 2004; also see review by Lorber, 2004). Recent studies suggest infant SNS activity associations with later behavior may depend upon other systems' functioning or environmental factors, such as lengthened resting PEP paired with greater surgency being associated with greater externalizing behaviors (Zhou et al., 2022) and both high and low SNS activity in infants relating to physical aggression on toddlers, but in a manner dependent upon PNS and environmental cumulative risk (Suurland et al., 2018). More work examining factors that shape the SNS in early childhood is needed if we are to understand its likely complex role in child outcomes and subsequent trajectories of health.

### *1.2. Prenatal stress and infant ANS*

Because the ANS plays a critical role in stress reactivity and regulation (Beauchaine, 2015) and is one mechanism through which exposure to early adversity affects emotional and behavioral outcomes, research examining the association between prenatal stress and infant ANS function is expanding (e.g. Bush et al., 2017; Gray et al., 2017). Such a focus aligns well with the origins of fetal programming research in cardiovascular disease (Barker, 1998) and evidence that variations in RSA have been associated with cardiovascular disease, the leading cause of mortality and morbidity in adults, as well as diabetes, obesity, and mental health outcomes (Arima & Fukuoka, 2020; Thayer & Lane, 2007). Further, late pregnancy and into the first year of life is a critical period in which offspring ANS is rapidly developing and vulnerable to adverse physiological and environmental pressures. For example, during this first year, critical connections are formed between the ANS and limbic system to integrate psychological and body responses (Mulkey & du Plessis, 2019), vagal myelination is continuing (Porges & Furman, 2011), and, overall, the infant brain doubles in size (Gilmore et al., 2018). Accordingly, exposures to adverse events in this sensitive period may have a potentially potent effect on ANS function across the life course (Porges & Furman, 2011), providing further rationale for this focus.

Our previous publication (Bush et al., 2017), reviews some of the literature demonstrating associations between prenatal stress and ANS function. In short, studies assessing ANS measures in infants have been primarily based on measures of PNS functioning such as HRV and RSA, or measures influenced by both the PNS and SNS, such as HR and heart period (HP). Although the field is expanding, the bulk of the original studies examining

prenatal stress effects on offspring ANS demonstrated associations between maternal stressors and fetal HR and HRV (see for review (Dipietro, 2012)), which has been shown to correlate with HR and HRV later in infancy (DiPietro et al., 2007). Although a host of studies report associations between maternal pregnancy mood or emotional health (depression and anxiety) and lower newborn resting vagal tone (an index related to HRV and RSA) (e.g. Abbott et al., 2018; Jacob et al., 2009; Propper & Holochwost, 2013; Van den Bergh et al., 2017; van Dijk et al., 2012), there are relatively few examinations of prenatal exposure to stressors, specifically, in the prediction of infant ANS outcomes. Although somewhat correlated, exposure to stress is distinct from psychopathology, and studies have found prenatal stress associations with offspring outcomes that are distinct from maternal depression (Ahmad et al., 2022; Van den Bergh et al., 2017; Walsh et al., 2019). Moreover, many prior studies examining prenatal stress have limited their examinations to resting levels of PNS rather than examining "stress reactivity" or changes in PNS functioning in response to stressors. For example, DiPietro et al. (2006) found that higher maternal rating of prenatal stress during pregnancy was associated with lower child vagal tone at age 2 within an upper-class sample of predominantly White women, although the association became marginal after infant sex was included. Jacob et al. (2009) found that the number of maternal life stressors was negatively correlated with neonatal resting HRV within a sample of 87 neonates born to low-income African American mothers, but maternal life stressors were not uniquely predictive in the full model. Although focused on mental health, rather than stress exposure, one of the few studies that assessed ANS reactivity found associations between maternal anxiety and lower vagal reactivity in boys (Tibu et al., 2014). Rash et al. (2016) found that mothers with greater psychological distress during late pregnancy were more likely to have infants who exhibited combined physiologic PNS and SNS reactivity profiles of co-inhibition (Rash et al., 2016). Because their results also report associations between prenatal stress (assessed at approximately the same time as the assessments made in this study), and ANS function across two branches (PNS and SNS), their findings are particularly worthwhile for comparison with the present study.

Other, related work has shown that perinatal poverty or low social support predicted muted HR and SNS reactivity trajectories from 6 months to 5 years of age in a sample of low-income Latino dyads (Alkon et al., 2014), and that higher levels of maternal cortisol (a hormone associated with stress arousal) during pregnancy were associated with lower infant resting RSA and higher RSA reactivity (Rash et al., 2015).

Very few studies examining prenatal stress and infant ANS have been conducted with the Still-Face Paradigm (SFP) (Tronick et al., 1978). The SFP, designed to evoke infant responses to parental interaction and disengagement, is one of the most widely used and validated measures to assess infant emotion regulation, and has been used in multiple studies to study infant ANS response (see Jones-Mason et al., 2018 for a review). Changes in ANS across the SFP are thought to reflect the infant's ability to marshal a sufficient biological response to challenge and to return to a regulated state after the challenge has ceased. Accordingly, infants will typically demonstrate lower RSA (PNS withdrawal) during the SF episode (the stressor of parental disengagement) and increased RSA (PNS activation) during reunion (Bazhenova et al., 2001; Moore & Calkins, 2004), though such patterns are most evident in primarily middle-class samples. Infants living in more adverse environments, however, may also show PNS

withdrawal during the SF but fail to increase RSA during reunion, or they may not show PNS withdrawal during the SF episode at all (Jones-Mason et al., 2018). The two SFP studies that examine prenatal stress effects on ANS suggest that infants whose mothers were exposed to higher levels of prenatal stress or earlier stressful life events show higher reactivity and/or difficulty recovering from challenge, demonstrated by a failure to return to baseline levels of RSA (Bush et al., 2017; Gray et al., 2017), higher reactivity during challenge (Bush et al., 2017), and lower RSA across the SFP (Gray et al., 2017).

The first to examine associations with both infant RSA and PEP, Suurland et al. (2016) reported that 6-month-old infants living in a home with low levels of maternal "psychosocial risk factors" (e.g. psychiatric disorder, substance use during pregnancy, or two or more of the following: no secondary education, unemployment, self-reported financial problems, limited or unstable social support network, single status, and maternal age under 20 years) showed RSA withdrawal during the SF episode and that both RSA and PEP increased (showing recovery) during reunion; infants raised in homes with higher psychosocial risk factors did not show a significant increase in RSA during reunion (in fact showed larger decreases in RSA across the SFP compared to low-risk infants), and PEP continued to withdraw across the SFP, with higher numbers of risk factors predicting greater PEP reactivity to the SF. Though informative, Suurland's findings were limited by the lack of adjustment for postnatal stress, and the probability that their "psychosocial risk factors" did not vary from pre- to 6 months postnatally, limiting the ability to conclude that observed effects were due to prenatal stress. Moreover, the predominantly sociodemographic factors within the cumulative risk score (e.g. unemployment, single status, and financial problems) in the context of a country that provides strong economic and social supports for pregnant and postpartum women might not necessarily carry the same "risk" consequences (and thus levels of stress) as they would in a country without such social supports. This, in addition to the overall low level of risk reported within the sample studied raise the question of whether the participants in the high-risk group felt particularly stressed.

In sum, there are several gaps in the literature examining associations between prenatal stress and ANS function in infants. First, there are limited research examining associations between prenatal stress and infant ANS, particularly examining ANS reactivity and especially lacking SNS functioning indicators. Reviews have acknowledged the limited research in this realm and called for further examination (Vehmeijer et al., 2019). Second, extant research has examined risk with a variety of measures and novel composites, limiting clarity when interpreting across studies. Third, much of the research on prenatal stress and ANS reactivity has been conducted outside of the United States and/or with predominantly middle or upper-class, White samples, limiting generalizability. Additional research on low-income, racially and ethnically diverse samples with substantial exposure to adverse life events is needed to confirm the conclusions of the limited extant research and advance our understanding of the impact of these factors during pregnancy on ANS function, across populations with inequitable exposure to harm. This research fills in some of those gaps by examining an understudied population, using independent coding of parental sensitivity in a widely used and validated measure, and particularly important, analysis of both infant PNS and SNS function in response to challenge and recovery contexts.

### 1.3. Prenatal stress and temperament

Temperament has been defined as "... constitutionally based individual differences in reactivity and self-regulation, as seen in the emotional, motor and attentional domains" (Rothbart et al., 2004, p. 357), which result from complicated interactions between environmental, genetic and other biological processes. Temperament may predict psychopathology and developmental trajectories (Van den Bergh et al., 2017). For example, higher "negativity (e.g. sadness, fear, discomfort, frustration, fidgeting, etc.) is associated with an increased risk of both internalizing and externalizing behaviors regulation/orienting predicts effortful control later in life (Gartstein et al., 2012). "Regulation" or "orienting" (e.g. comprised of scales assessing low-intensity pleasure, duration of orienting, and soothability) (Gartstein & Rothbart, 2003) predicts effortful control later in life, preschool behavioral issues, as well as externalizing and internalizing behaviors (Gartstein et al., 2012).

Although results are mixed, in general, higher prenatal stress is associated with greater negativity and poorer regulation in offspring (see review Van den Bergh et al., 2017). Some studies have reported null associations with infant mood or negativity, however (Bush et al., 2017; Lin et al., 2017). As in the ANS literature, these mixed results suggest that other factors may modify the association between prenatal stress and infant temperament, including postnatal influences.

### 1.4. Parenting sensitivity and infant ANS

A growing literature has reported that the presence of the parent lowers infant physiological reactivity in times of threat, but this literature has primarily focused on cortisol measurement, leading to the development of a broad literature confirming and documenting the social regulation of the hypothalamic – pituitary–adrenal axis (HPA) through parenting and other sensitive caregivers (Albers et al., 2008; Berry et al., 2017; Braarud & Stormark, 2006; Brown et al., 2020; Gunnar et al., 1996; Hostinar et al., 2014; Nachmias et al., 1996; Yirmiya et al., 2020). As a result, there are a number of SFP studies demonstrating how "positive parenting" predicts decreases in infant cortisol reactivity (Grant et al., 2009; Haley & Stansbury, 2003; Martinez-Torteya et al., 2014). The literature examining the association between parenting behaviors and infant ANS, however, is less common but growing. A recent review and meta-analysis of SFP studies which included discussion of associations between various parenting constructs, such as parental "sensitivity" or "responsiveness," and infant ANS (Jones-Mason et al., 2018) found that, generally, infants of insensitive or nonresponsive parents had lower RSA during reunion than the infants of more sensitive or responsive parents suggesting poorer vagal regulation. The very few studies that examine infant SNS function in this context report that the SNS is activated across the SFP (Ham and Tronick, 2006), that skin conductance (SC) concordance is positively associated with mother-infant behavioral synchrony (Ham & Tronick, 2009), and that SNS activation during the SF episode is associated with maternal insensitivity during play and reunion (Bosquet Enlow et al., 2014).

Other studies outside of the SFP have also reported correlations between parental sensitivity, or related constructs, and ANS (Alen et al., 2022). Although these results are mixed (Burgess et al., 2003), some studies report that PNS withdrawal is positively associated

with parental sensitivity (Perry et al., 2014, 2016). Given the association between heightened parental sensitivity and security of attachment (De Wolff & van Ijzendoorn, 1997), attachment studies are also informative. For example, one study found that parent–child attachment insecurity is associated with delayed child HR deceleration in reunion, higher vagal withdrawal and limited RSA recovery (Hill-Soderlund et al., 2008). A different study reported that children classified as insecure showed lower RSA across the strange situation paradigm (SSP) while secure children showed no change in ANS (Smith et al. (2016)). Very few studies examine infant SNS activity, however. Among relevant extant parental sensitivity studies of young children, one-year-olds with mothers that displayed high levels of disruptive behaviors showed higher SNS activation during challenge (Kohler-Dauner et al., 2019), while two-year-old children in foster care with a history of parental neglect showed the highest SNS reactivity during challenge (Oosterman et al., 2010). Overall, although the weight of the evidence suggests that parental sensitivity is linked with infant PNS withdrawal during challenge and PNS augmentation during reunion, there are great gaps in the infant ANS literature, including the lack of sociodemographic diversity in samples, the lack of studies on the association between sensitivity and infant SNS, and the limited studies examining RSA and PEP reactivity and recovery. Even less understood is the potential buffering role of parenting for the association between pregnancy stress and infant physiological reactivity and regulation.

### *1.5. Parenting and temperament*

Although temperament is not the result of relational interactions, temperament may be modified by experience, including social relationships (Vaughn & Bost, 2016). Because temperament is less stable in infancy, the impact of caregiving might be most observable during this period (Parade et al., 2017). Accordingly, a number of studies have examined the effects of parenting on infant temperament. For example, studies have reported that maternal sensitivity during the SFP reunion was inversely related to infant-negative temperament in a low-SES sample of mothers (Conradt & Ablow, 2010). Studies that included middle- or upper-class subjects reported that higher maternal intrusiveness was associated with difficult infant temperament (Parade et al., 2017), and that higher maternal sensitivity was associated with lower increases in fear reactivity from 4 to 16 months of age (Braungart-Rieker et al., 2010), lower negativity, and higher positive affect, orienting toward parent, and self-comforting in 5- and 7-month-old infants (Braungart-Rieker et al., 2014). Other studies reported that higher parental sensitivity was associated with lower infant fear or negative emotionality (Pauli-Pott et al., 2004), and lower levels of infant emotional distress and increased behavioral recovery from the SFP (see Mesman et al., 2009 for review). Accordingly, the weight of the research appears to report negative associations between sensitivity and infant negativity and positive associations between sensitivity and regulation.

In sum, the literature examining associations between parental sensitivity and ANS or temperament still predominately involves middle/upper-class White populations. Further research on low-income, racially and ethnically diverse samples with substantial exposure to adverse life events is needed to confirm the conclusions of the limited extant research, extend generalizability of the findings, and advance our understanding of the likely impact of these prenatal stress factors on offspring early life ANS function and temperament.

## 2. The present study

To address the need for a deeper understanding of the contexts in which prenatal stress exposure may predict infant physiological and behavioral functioning, this study extends our previous work in an understudied population (Bush et al., 2017) in several important ways. Considering the substantial variability in the association between prenatal stress and infant reactivity and regulation, and because parenting is a key protective factor in contexts of stress, the present study tested whether objectively coded parenting behaviors assessed during the SFP modify the association between prenatal stress and 6-month-old infant ANS functioning or temperament. Further, the study includes an examination of these associations in the prediction of infant SNS functioning, filling a void in infant developmental research. This study used reports of stressful life events experienced during pregnancy because the literature suggests (although the research is mixed) that measures reporting exposure to stressful events may be stronger predictors of negative infant outcomes than accounts of subjective short-term perceived stress (DiPietro et al., 2006; Felder et al., 2020) and have been associated with child mental health in large, national samples (Bush et al., 2023; LeWinn et al., 2022; Norona-Zhou et al., 2023).

Two hypotheses were formulated based on the extant research. First, we expected that higher parental sensitivity would buffer the association between maternal prenatal stress exposures and infant outcomes. Specifically, it was hypothesized that prenatal stress exposures would be 1) positively associated with ANS (RSA and PEP) reactivity and negative temperament, and 2) negatively associated with ANS (RSA and PEP) recovery and temperamental regulation, but only in the context of low parental sensitivity. Second, in cases where no interaction was detected, we hypothesized there would be a main effect of parental sensitivity on infant outcomes, such that higher levels of coded parental sensitivity would be associated with lower ANS (RSA and PEP) reactivity and higher recovery, lower infant negativity and higher infant regulation.

## 3. Methods

### *3.1. Participants and procedures*

Study participant dyads were drawn from a nonrandomized control trial that was designed to examine the effects of a group-based, mindfulness stress reduction and healthy lifestyle intervention called MAMAS (Maternal Adiposity, Metabolism, and Stress Study) (Epel et al., 2019). Both intervention and treatment-as-usual participants were followed longitudinally. Additional details about the study as well as the recruitment strategy have been published previously (Coleman-Phox et al., 2013). Inclusion criteria included that women be in their second trimester of pregnancy (12–24 weeks) with a singleton pregnancy, English-speaking, with a pre-pregnancy body mass index of 25–41 kg/m2, household income less than 500% of the federal poverty level (e.g. $73,550 for a family of two in 2011, a US indicator of low to middle income; US Department of Health and Human Services, 2013), and without medical conditions that might affect gestational weight gain. SEED initially recruited 215 women for the pregnancy study. There were no differences in baseline characteristics or prenatal stress between the 162 women who

consented to postnatal follow-up via the SEED study, compared to those who declined or who were lost to follow-up (Bush et al., 2017). Of the 162 enrolled, 155 participants agreed to the 6-month in-person visit and completed when the infant was between 6 and 9 months of age. One participant was missing behavioral outcome data and thus was excluded from analyses, leading to a possible SEED sample of 154 infants at this time point. Delays in NIH processing of funding for SEED prevented us from being able to collect physiologic data on 6-month-old infants born to women in the first half of the MAMAs cohort. After refinement of the ANS collection protocol and piloting its administration with this sample, a total of 66 infants completed the ANS assessment within the standardized paradigm and had sufficient ANS data for analysis. A CONSORT diagram outlines study sample participation in Figure 1. Table 1 provides descriptive information on the full offspring study sample and subsample with infant ANS data.

At 6 months of age, all infants were living in households with their biological mothers. Maternal self-reports were used to determine maternal age, parity, marital or partnered status, race and ethnicity, education, annual household income, and number of individuals in the household. As noted in prior publications (Bush et al., 2017) there were no differences in maternal characteristics between those mothers with or without infant ANS outcomes.

This study focuses on measures assessed during the second half of pregnancy ($M$ = 25.6 weeks, SD = 4.5) and at 6 months postpartum. Trained research assistants (RAs) reviewed medical records to abstract data and confirm gestational age and birth weight. The infant experimental stress paradigm was conducted in person, either in the clinic or in participants' homes, in conjunction with the maternal assessment during the 6-month postpartum visit (M infant age = 6.5 months, SD = 0.6 months); visits were scheduled on days and times mothers felt their infant was well rested and fed and could be alert for the

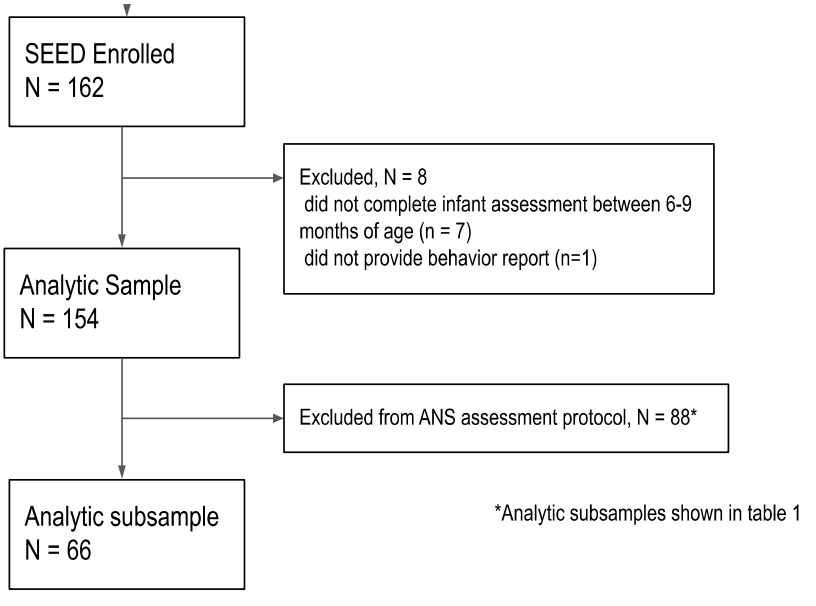


Figure 1. SEED study consort diagram.

**Table 1.** Descriptive information for sample and subsample of children with ANS data.

| | | Analytic Subsample | | |
|---|---|---|---|---|
| | Full Sample (*N*=140–154) | No ANS data (*N*=69–88) | ANS data (*N*=54–66) | *p* |
| Infant | | | | |
| Gestational Age (days) | **277.2 (10.0)** | 278.2 (10.1) | **275.9 (9.8)** | 0.2 |
| Birthweight (kg.) | **3.4 (0.5)** | 3.4 (0.5) | **3.3 (0.4)** | 0.6 |
| % Female | **51%** | 51% | **52%** | 0.9 |
| Ethnicity | | | | |
| % Hispanic | **38%** | 33% | **45%** | 0.2 |
| Race[a] | | | | |
| % Black | **35%** | 40% | **29%** | |
| % White | **19%** | 14% | **26%** | |
| % Asian | **3%** | 5% | **2%** | |
| %Native Hawaiian or other Pacific Islander | **1%** | 1% | **0%** | |
| % American Indian or Alaska Native | **1%** | 1% | **2%** | |
| % Middle Eastern or North African | **1%** | 1% | **2%** | |
| % Multiracial | **24%** | 20% | **29%** | |
| % Other | **16%** | 18% | **12%** | |
| Maternal | | | | |
| Maternal Age (years) | **28.0 (5.7)** | 27.7 (5.4) | **28.3 (6.0)** | 0.5 |
| Parity (% first born) | **45%** | 45% | **45%** | 0.9 |
| % Married/Partnered | **68%** | 65% | **72%** | 0.4 |
| Income[b] | **$19,200 range: $0–86,000** | $19,200 range: $0–78,000 | **$19,500 range: $0–$86,000** | 0.3 |
| Percent Poverty | **139.1 (114.9)** | 133.2 (112.1) | **146.7 (119.0)** | 0.5 |
| PSS Postnatal | **1.5 (0.7)** | 1.4 (0.7) | **1.6 (0.70)** | 0.3 |
| SLE Count | **2.6 (2.1)** | 2.4 (2.0) | **2.8 (2.3)** | 0.2 |
| PHQ Postnatal | **4.5 (4.0)** | 4.3 (4.2) | **4.9 (3.8)** | 0.3 |

Mean (SD) or [b]Median/w Range for continuous variables; % sample for categorical variables.
[a]Race categories were collapsed to Black, White, Multiracial and Other for subsample comparison test. PHQ means Patient Health Questionnaire. Percent Poverty means percent of the US federal poverty level.

activities. Note that further, analyses revealed no difference in ANS values by home or clinic, consistent with other home/clinic infant ANS studies (Haley et al., 2006). All procedures were approved by the Institutional Review Board at the University of (Protocol No. 10–04522-SEED).

## 3.2. Measures

### 3.2.1. Stressful life events (SLE)

Maternal report of the number of prenatal objective stress exposures was assessed retrospectively approximately 6 months after delivery. Stressful life events (SLE) were assessed with a list of 14 events adapted from the PRAMS survey (Centers for Disease Control and Prevention CDC, 2005; Senter et al., 2021), a population-based postpartum survey of maternal attitudes and experiences before, during, and after pregnancy (covering approximately 12 months prior to the birth of the child). Participants were asked to respond yes or no to statements about experiences with illness, death, relationship problems, housing difficulties, legal issues, and financial problems during pregnancy. Affirmative responses were summed. The number of SLE reported ranged from 0 to 8, with 14% reporting no events, 39% reporting 1 or 2 events, and 47% reporting 3 or more events. The mean SLE count was 2.6 (SD = 2.1). Such measures of

events are thought to have limited recall bias and be accurate over a span of years (Krinsley et al., 2003). Maternal report of perceived stress was considered a covariate (described below) in the present study.

### 3.2.2. Infant stress paradigm

The SFP provides a structured protocol designed to elicit infant self-regulation in response to parental interaction and disengagement. The SFP has shown good re-test reliability (Provenzi et al., 2016) and good construct validity and has been used to examine a number of developmental phenomena (see for review Mesman & Emmen, 2013).

The SFP was administered during the 6-month visit. The standard SFP consists of a sequence of three, 2-min episodes (play, Still Face [SF], and play) in which the parent and the infant are seated about 1 m away from each other. During the first "play" episode, the parent is instructed to play "naturally" with the child as they normally would without toys. During the SF episode, the parent is asked to maintain a neutral expression on her face and is told not to touch or interact with the baby. The third episode, sometimes referred to as the "reunion" episode, is a resumption of play in which the parent is told to respond to the infant in the manner they choose but without removing the child from the seat. For the (name withheld) study, infant – mother dyads participated in a 10-min SFP protocol including five episodes: 2-min play (baseline); 2-min SF (SF 1); 2-min play (Reunion 1), as well as a 2$^{nd}$ 2-min SF (SF2) and 2-min play (Reunion 2), which have been shown to enhance infant stress responses (e.g. Bosquet Enlow et al., 2014). Mothers were told that they could discontinue the task at any point if they felt the infant was overly stressed. RAs were also trained to terminate the task if the infant demonstrated significant distress for longer than 1 min and the mother had not chosen to terminate. Note that the present study only utilized data from the first three episodes due to concern about the considerable distress-related drop-out of infants in the latter episodes, within the already small ANS subsample, and the number of analyses being conducted without the addition of models using those episodes.

### 3.2.3. Parental sensitivity

Maternal behavior was videotaped during the play and reunion episodes of the SFP. Note that coding in the SFP does not globally evaluate parental sensitivity but rather, using attachment-related constructs, assesses parental behaviors that are elicited by an infant subjected to the specific stressor of parental disengagement. Here, two trained researchers masked to infant ANS and temperament and maternal stress variables coded maternal behavior using 5-point Likert ratings from the MACY (Maternal Anxiety in the Childbearing Years) Infant-Parent Coding System (Earls et al., 2009) (MIPCS). The MIPCS coding system has roots in attachment theory and was specifically designed for rating parent, infant and dyadic interactions during tasks such as the SFP, unstructured play or teaching measures. The MIPCS scales significantly correlate with parental reflective functioning, a construct related to parental sensitivity and associated with infant attachment security (Fonagy et al., 2002), as well as the Strange Situation Procedure (SSP) (Stacks et al., 2014). Specifically, the study used scales designed to assess maternal sensitivity (e.g. the mother's understanding of or ability to recognize communications from her infant as demonstrated by sensitive vocalizations, facial expression, physical handling responses, empathetic responses, etc.), flexibility (e.g. the degree to which the mother is resourceful,

creative, and flexible in handling her infant's distress), engagement (e.g. the degree to which the mother engages in play with her infant demonstrated by behaviors such as pacing, body position and vocalizations), and parental success in calming infants (i.e. "regulation"). These scales were significantly correlated (Pearson correlations ranged from 0.324 to 0.801). Thus, they were combined into one "parental sensitivity" index (hereinafter "sensitivity") by averaging the ratings of the maternal scales, following similar practices in other studies (Martinez-Torteya et al., 2014). Hostility (e.g. the frequency, duration, and intensity of the parent's rejection, hostility, and/or ambivalence during infant–parent interactions) and intrusiveness (e.g. the degree to which parental behavior *interferes with* the infant's goals) were also assessed, which for theoretical reasons were combined into an index of "negative parenting." Analyses examining negativity as a modifier were not pursued in final analyses, however, due to limited variability in this domain ($M = 1.48$, SD = .61) and the small number of maternal participants displaying negativity. This study focused on sensitivity assessments in reunion because of documented associations between sensitivity in the SFP reunion and ANS function (Conradt & Ablow, 2010) and theoretical assertions that sensitivity to bids for safety/protection should be more predictive of attachment-related phenomenon because the central purpose of the attachment system is the protection of offspring (Leerkes et al., 2009). Inter-coder reliability was assessed using intra-class correlations (ICC) on 77 videotapes of 32 randomly selected participants. The ICC for maternal coding across the SFP (Play 1, 2 and 3) was .909 demonstrating good to excellent inter-coder reliability. Our ICC results were generally within the range reported by other studies that have used the MACY scales (Julian et al., 2019; Martinez-Torteya et al., 2015)

#### *3.2.4. Infant temperament*

At 6 months postpartum, mothers completed the Infant Behavior Questionnaire – Revised (IBQ-R), a measure designed to assess temperament in infants between 3 and 12 months of age. Parents are asked to rate how often they observed a particular behavior in their infant within the last 1 to 2 weeks, on a 7-point scale ranging from 1 (never) to 7 (always). The 91 items load onto 14 scales with very good internal reliability (ranging from .70 to .90 for parent report; (Gartstein & Rothbart, 2003)). In line with common practice, two "super-factor" composite variables were created, all demonstrating good internal consistency in this sample. Infant *regulation* was computed from the mean scores of the approach, vocal reactivity, high-intensity pleasure, smiling, and laughter; activity level; and perceptual sensitivity subscales (α= .79). Infant *negativity* was computed from the mean scores of the sadness, distress to limitations, fear, and falling reactivity subscales (α= .85).

#### *3.2.5. ANS*

To obtain measures of children's PNS and SNS activity, we assessed RSA and PEP, respectively. RSA is a reliable index of the PNS influence on cardiac functioning in adults (Bernston et al., 1993) and in child and adolescent samples (Alkon et al., 2006; Calkins & Keane, 2004). PEP is a similarly reliable index of SNS in child, adolescent and adult samples (Alkon et al., 2014; Suurland et al., 2016). RSA indices were calculated using the interbeat intervals detected from electrocardiography (ECG) readings, respiratory rates detected from impedance waveforms (e.g. dZ/dt), and a bandwidth range of 0.15 to 1.04 Hz for 6-month-olds (Bar-Haim et al., 2000) collected continuously using BioNex hardware and

BioLab acquisition software version 3.0 (Mindware Technologies, Ltd., www.mindwaretech.com) from infants throughout the SF protocol. PEP time intervals were calculated based on the time in milliseconds from the ECG Q-point (corresponding to the onset of ventricular depolarization) to the B-point of the dZ/dt waveform (corresponding to the onset of left ventricular ejection). A full description of the ANS collection, scoring, and cleaning methodology used in this study timepoint has been described previously (Bush et al., 2016, 2017).

As noted earlier, analyses here focus on the first three episodes of the SFP task, as the latter two had significant distress-related dropout and led to very low sample sizes (Bush et al., 2017). To enhance the reliability of our estimates of RSA and PEP for the target episodes (e.g. play 1 and SF 1), reactivity analyses were focused on participants with three or more scorable RSA and PEP 30-second (s) episodes (the episode averages were created by averaging three or four 30-s epochs) within the play and SF1 episodes. However, because of distress-related dropout in response to the SF1 episode, we used all available data to analyze recovery (reunion 1 – play 1). Of the 66 children with usable ANS data, a total of 66 had scorable RSA and PEP in the play episode, and 61 had scorable RSA and 62 had scorable PEP in the SF episodes. Fifty-five had scorable RSA or PEP data for the reunion episodes. Table 2 presents the descriptive information for RSA and PEP levels across the three SFP episodes, as well as the mean RSA and PEP reactivity and recovery values across the paradigm. SF RSA and PEP *reactivity* scores were calculated by subtracting the average response during the first 2-min play episode (baseline) from the average response across the stressor task (SF 1). To ascertain recovery, we used change scores (ANS in reunion-ANS in Play) as our outcome variable, a common practice in the literature (Jones-Mason et al., 2018).

### 3.2.6. Covariates

Because of the theoretical or empirical potential for confound, poverty, child sex, and pregnancy intervention group classification (heretofore "intervention," indicated as either part of the group-based intervention or treatment-as-usual group) were included in all analyses although they were not all significantly correlated with every outcome of interest. Note that for the poverty covariate participants reported total household income and number of individuals living in the household at enrollment. Household income was converted to percent of the US federal poverty level (US Department of Health and Human Services, 2011).

**Table 2.** Descriptives for ANS variables across the SFP episodes.

| | | Episode-Level Values | | Difference Score Calculations | | | |
|---|---|---|---|---|---|---|---|
| | Episode | N | Mean (SD) | N | Mean Change | t-test | Paired test |
| RSA | Play | 66 | 4.29 (1.05) | | | | |
| | SF | 61 | 4.0 (1.23) | 61 | −.24 (.97) | 1.95[t] | SF 1 – Play 1 |
| | Reunion | 55 | 3.85 (1.44) | 55 | −.40 (1.23) | −2.45*** | Reunion – Play1 |
| PEP | Play | 66 | 75.98 (5.26) | | | | |
| | SF | 62 | 75.58 (5.45) | 62 | −.40 (2.03) | −1.6 | SF 1 – Play 1 |
| | Reunion | 55 | 74.46 (5.86) | 55 | −1.32 (2.34) | −4.18*** | Reunion– Play1 |

[t]= $p < .10$, * = $p < .05$, ** = $p < .01$, ***=p<.001. Mean change for reunion refers to the difference between reunion and play. Mean change for the SF refers to the difference between the Still Face (SF) and play.

Although pregnancy prenatal stress exposures are likely to result in sustained distress, in order to increase confidence in the prenatal timing of effects examined, all models also controlled for postnatal maternal stress using the Perceived Stress Scale (PSS) (Cohen et al., 1983). The PSS assesses an individual's perceptions of his or her generalized stress and coping over the previous month (as opposed to reactions to a specific event). The PSS assesses current levels of stress and the extent to which individuals perceive their lives as "unpredictable," "uncontrollable," and "overloaded." Participants responded to 10 items asking how often they had certain thoughts and feelings in the last month on a 5-point scale (never, almost never, sometimes, fairly often, and very often). Positively worded items were reverse-coded. Although the PSS was administered twice during pregnancy and again at the 6-month visit we use only postnatal PSS in this analysis primarily to avoid problems with multicollinearity (reports were correlated .528–.660 across time) and due to the desire to emphasize adjustment for perceived stress at the time of outcome measurement. Internal consistency was good (0.85). In addition, because we previously found associations between pre/postnatal maternal mood variables, including maternal perceived stress (assessed with the PSS) and depression (assessed with the Patient Health Questionnaire (PHQ) (Kroenke et al., 2001)), and IBQ subscales, we also tested the impact of adding postnatal PSS or PHQ to all models predicting temperament. Note that to preserve power in models predicting ANS, postnatal PHQ was not included because bivariate analyses showed no correlation between postnatal PHQ and ANS.

Finally, as noted above, this sample consisted of women who reported being overweight or obese pre-pregnancy. Notably, approximately 70% of the adult population in the United States (66.2% of women, 73% of men) is either overweight (BMI = 25 to <30) or obese (BMI = 30 or higher), and rates are even higher among women of color (82% of African Americans, 77.1% of Latinas/Hispanics) (Centers for Disease Control and Prevention CDC, 2016; Flegal et al., 2016). Although national rates of overweight-obese status suggest our sample is not exceptional in this regard, we considered whether BMI might confound associations. Bivariate analyses showed that maternal BMI was not significantly associated with parenting or any of our outcomes of interest. Accordingly, we did not retain maternal BMI as a covariate to preserve power and best align with prior published models by other labs in this domain.

### *3.2.7. Power calculation*

Using an alpha level of 0.05, with 80% power, and assuming a Cohen's effect size of 0.2, we estimated that we would need a sample size of approximately 60 to detect significant effects using linear regression, assuming two primary exposures and one moderation predictor being tested along with 3 covariates. Given our largest possible sample ($N$ = 154), we estimated power between 70% and 80% to detect a significant interaction. Assuming an effect size of 0.2 for the interaction, a weak correlation between exposures ($r$ = .1), and a range of effect sizes for primary exposures between .2 and .4, our sample may be underpowered to detect true *small* effects, suggesting observed significant results may be limited to small-to-moderate effects.

#### 3.2.8. Data analysis

Analyses were performed using R version 4.2.2. Data were assessed for normality and potential outliers. First, descriptive statistics and bivariate Pearson correlations between prenatal and postnatal stress (SLE and postnatal PSS) and depression (postnatal PHQ), sensitivity, ANS in SFP (play 1, SF, reunion, reactivity and recovery), IBQ negativity and regulation and maternal pre-pregnancy BMI were performed. Second, interaction terms created from cross-product predictor variables were used to create the primary linear regression models that examined whether sensitivity moderated the association between prenatal stress and a) ANS reactivity, b) ANS recovery and c) IBQ factors, including covariates as described above. After adding all relevant covariables for the complete-cases analyses, analytic sample sizes were 48 and 47 for ANS reactivity and recovery outcomes, respectively, and 99 for temperament outcomes. To address concerns about missingness and reduced power, the mice (Multivariate Imputation by Chained Equations) package in R (van Buuren and Groothuis-Oudshoorn, 2011) was used to impute missing values for all missing predictors, separately for each analytic sample. For the behavior outcome sample, missing data across exposures and covariates ranged from 3% to 20%. For the ANS sample, missing data ranged from 1% to 20%. The imputation model used all other variables as predictors for each incomplete data variable, including coded sensitivity and prenatal stress interaction terms. Sample sizes for pooled regression results were 66 for ANS and 154 for IBQ factors. Outcome variables and maternal sensitivity were standardized before modeling. ANS reactivity and recovery were coded so that larger values indexed greater reactivity and greater recovery, respectively.

The Johnson-Neyman (JN) bootstrapping technique was used to provide the values within the range of the moderator (i.e. parental sensitivity) in which the association between prenatal stress and ANS function or infant temperament was significant. The JN technique reveals whether the predictor's (x) effect on the outcome (y) differs from zero at some values of the moderator, but only the interaction determines whether the conditional effects of x significantly differ from each other. Conditional effect plots are provided to illustrate regions of significance for selected examples. Post-hoc probing on select associations was conducted using estimation of simple slopes to illustrate patterns of findings. As a follow-up, in cases where interaction terms were not significant, a sensitivity analysis was performed, and we note main effects with the interaction term dropped.

Finally, to adjust for multiple testing, we applied the False Discovery Rate (FDR) to interaction tests using the Benjamini and Hochberg (1995) procedure. We adopted a q value boundary (the proportion of tests below which are false positives) of .05. FDR was applied to all interaction results.

## 4. Results

### 4.1. Preliminary analyses

Previous reports on this cohort compared dyads in the ANS subsample to the subsample without usable ANS data on the key maternal stress predictor variables and covariates poverty, gestational age and birth weight; the subsample was representative of the larger sample, and there were no significant differences between those with

and without ANS data on maternal stress (Bush et al., 2017). Descriptives for the full sample and for the sample split by availability of ANS data are also provided in (Bush et al., 2017)). Descriptive statistics for infant RSA and PEP values by SFP episode, and paired t tests for means across episodes are presented in Table 2. As presented in Table 2, RSA decreased between play and the SF episode but did not reach statistical significance ($p < .10$). On average, no significant difference in infant RSA between SF and reunion was detected, although there was considerable variability in levels of RSA change. RSA in reunion was lower than RSA in play ($t = -2.45$, $p < 0.001$). No significant difference in PEP between the play and SF episodes was detected, but PEP did significantly *shorten* from SF episode to reunion ($t = -3.249$, $p = 0.002$). On average, PEP during reunion was shorter (i.e. SNS activation) than in play ($t = -4.18$, $p < 0.001$). These patterns of ANS reactivity suggest continuing reactivity throughout the SFP and are consistent with other studies of cohorts reporting high-stress levels (Jones-Mason et al., 2018). Bivariate correlations are provided in Table 3. Of note, prenatal stress was not correlated with parenting codes or any ANS measures. Several significant correlations emerged between the measures of parenting and infant ANS and temperament, providing support for examining these associations in fully adjusted models. Note that, consistent with prior literature, sensitivity was lower in reunion ($M = 3.97$, $SD = .87$) than in the play episode ($M = 4.13$, $SD = .85$) perhaps, as suggested by some researchers, because more parents may be able to demonstrate sensitivity toward the infant during non-stressful conditions than are able to do so during times of stress or challenge (Bosquet Enlow et al., 2014; Conradt & Ablow, 2010). Despite the difference, sensitivity in play and reunion was strongly positively correlated ($r = .51$, $p < .001$), providing additional evidence for continuity of maternal behavior across episodes as well as support for the validity of the sensitivity measure (Conradt & Ablow, 2010). Consistent with previous research, sensitivity was positively associated with higher RSA and longer PEP throughout the SF and reunion episodes.

### 4.2. Tests of parenting as a moderator of the effects of prenatal stress on infant outcomes

Table 4 shows the results of regression analyses testing whether sensitivity modifies the association between SLE and ANS reactivity and recovery while controlling for infant sex, poverty and prenatal intervention status.

Any significant changes to associations found in primary temperament models due to inclusion of postnatal depression are described below. As noted, significant main effects of sensitivity are only described in the context of non-significant interactions. Findings for models predicting ANS reactivity and recovery are plotted (Figure 2) and provide regions of significance for the moderating effects of maternal sensitivity on associations between SLE and infant outcomes. To illustrate the parallel patterns of moderated association and consistency of effects found, illustrations of the simple slopes for the association between SLE and ANS reactivity and recovery across both branches of the ANS, plotted across terciles (at low, average, and high levels) of parental sensitivity are provided in Figure 3. Results from the missing data imputation (MI) models are presented in S1. In line with the proposed aims of this study, models were run with parenting as the moderator (or buffer for stress effects); however, for interested readers, regions of significance and simple slopes are also presented

**Table 3.** Bivariate correlations between primary model variables, as well as foundational study variables and covariates considered.

| | | Sensitivity | SLE | RSA Reac. | PEP Reac. | RSA Rec. | PEP Rec. | Negativity | Regulation |
|---|---|---|---|---|---|---|---|---|---|
| Sensitivity | Pear. Corr. | 1 | | | | | | | |
| | Sig. | | | | | | | | |
| | N | 123 | | | | | | | |
| SLE | Pear. Corr. | 0.07 | 1 | | | | | | |
| | Sig. | 0.35 | | | | | | | |
| | N | 116 | 145 | | | | | | |
| RSA Reactivity | Pear. Corr. | 0.30* | −0.21 | 1 | | | | | |
| | Sig. | 0.03 | 0.12 | | | | | | |
| | N | 52 | 57 | 59 | | | | | |
| PEP Reactivity | Pear. Corr. | 0.26 | −0.05 | .46** | 1 | | | | |
| | Sig. | 0.06† | 0.72 | 0.01 | | | | | |
| | N | 52 | 57 | 59 | 59 | | | | |
| RSA Recovery | Pear. Corr. | .56** | −0.05 | .49** | .09 | 1 | | | |
| | Sig. | 0.01 | 0.73 | 0.01 | .49 | | | | |
| | N | 51 | 53 | 55 | 55 | 55 | | | |
| PEP Recovery | Pear. Corr. | .46** | −0.07 | .44** | .54** | .53** | 1 | | |
| | Sig. | 0.01 | 0.61 | 0.01 | .01 | 0.01 | | | |
| | N | 51 | 53 | 55 | 55 | 55 | 55 | | |
| Negativity | Pear. Corr. | −.20* | 0.06 | −0.17 | −.13 | −0.23 | −.28* | 1 | |
| | Sig. | 0.02 | 0.45 | 0.19 | .31 | 0.09† | .04 | | |
| | N | 122 | 144 | 59 | 59 | 55 | 55 | 154 | |
| Regulation | Pear. Corr. | 0.15 | 0.03 | 0.08 | .13 | 0.24 | .17 | −.337** | 1 |
| | Sig. | 0.15 | 0.76 | 0.55 | .34 | 0.07† | .22 | 0 | |
| | N | 122 | 144 | 59 | 59 | 55 | 55 | 154 | 154 |
| RSA P1 | Pear. Corr. | 0.02 | 0.09 | −0.28* | −.11 | −0.15 | −.20 | −0.09 | 0.01 |
| | Sig. | 0.87 | 0.51 | 0.03 | .41 | 0.27 | .14 | 0.47 | 0.93 |
| | N | 53 | 62 | 59 | 59 | 55 | 55 | 65 | 65 |
| PEP P1 | Pear. Corr. | 0.20 | −0.01 | 0.02 | −.15 | 0.21 | .12 | −0.30* | 0.19 |
| | Sig. | 0.16 | 0.95 | 0.90 | .26 | 0.13 | .40 | 0.01 | 0.12 |
| | N | 53 | 62 | 59 | 59 | 55 | 55 | 65 | 65 |
| RSA SF | Pear. Corr. | .28* | −0.11 | 0.59** | .29* | 0.30* | .22 | −0.28 | 0.08 |
| | Sig. | 0.04 | 0.40 | 0.01 | .03 | 0.02 | .11 | 0.03* | 0.52 |
| | N | 52 | 57 | 59 | 59 | 55 | 55 | 59 | 59 |
| PEP SF | Pear. Corr. | .31* | −0.03 | 0.20 | .25 | 0.25 | .34* | −0.34** | 0.26 |
| | Sig. | 0.03 | 0.85 | 0.13 | .06† | 0.07† | .01 | 0.01 | 0.05* |
| | N | 52 | 57 | 59 | 59 | 55 | 55 | 59 | 59 |
| RSA Reunion | Pear. Corr. | .50** | −0.00 | 0.21 | −.07 | 0.75** | .31* | −0.25 | 0.19 |
| | Sig. | 0.01 | 0.98 | 0.13 | .62 | 0.01 | .02 | 0.07† | 0.18 |
| | N | 51 | 53 | 55 | 55 | 55 | 55 | 55 | 55 |
| PEP Reunion | Pear. Corr. | .35* | −0.03 | 0.18 | .02 | 0.39** | .50** | −0.37** | 0.26 |
| | Sig. | 0.01 | 0.84 | 0.20 | .89 | 0.01 | .01 | 0.01 | 0.06† |
| | N | 51 | 53 | 55 | 55 | 55 | 55 | 55 | 55 |
| Intervention | Pear. Corr. | 0.03 | −0.15† | −0.01 | −.29* | 0.10 | −.06 | 0.08 | −0.02 |
| | Sig. | 0.78 | 0.08 | 0.93 | .02 | 0.47 | .68 | 0.35 | 0.82 |
| | N | 123 | 145 | 59 | 59 | 55 | 55 | 154 | 154 |
| Poverty | Pear. Corr. | −0.00 | −.27** | −0.06 | .03 | 0.03 | −.20 | −0.15 | 0.05 |
| | Sig. | 0.99 | 0.01 | 0.65 | .83 | 0.85 | .15 | 0.07† | 0.56 |
| | N | 116 | 138 | 57 | 57 | 53 | 53 | 147 | 147 |
| Sex*** | Pear. Corr. | −0.03 | 0.22** | −0.01 | −.24 | 0.08 | −.23 | 0.21** | 0.05 |
| | Sig. | 0.76 | 0.01 | 0.97 | .07† | 0.58 | .09† | 0.01 | 0.58 |
| | N | 123 | 145 | 59 | 59 | 55 | 55 | 154 | 154 |
| PN PSS | Pear. Corr. | 0.07 | 0.15 | 0.16 | .19 | 0.01 | −.08 | 0.21* | −0.15 |
| | Sig. | 0.44 | 0.08 | 0.24 | .15 | 0.92 | .56 | 0.04 | 0.08† |
| | N | 112 | 131 | 58 | 58 | 55 | 55 | 139 | 139 |
| PN depression | Pear. Corr. | 0.06 | 0.20* | 0.09 | .12 | 0.00 | −.01 | 0.22** | −.27** |
| | Sig. | 0.53 | 0.02 | 0.52 | .38 | 0.99 | .96 | 0.01 | 0.01 |
| | N | 113 | 132 | 58 | 58 | 55 | 55 | 140 | 140 |
| PP BMI | Pear. Corr. | 0.03 | 0.06 | 0.10 | .08 | 0.23 | .13 | 0.06 | 0.11 |
| | Sig. | 0.75 | 0.47 | 0.47 | .55 | 0.09† | .34 | 0.44 | 0.17 |
| | N | 123 | 145 | 59 | 59 | 55 | 55 | 154 | 154 |

**$p$</=.01, *$p$</=.05, †p<.10 (two tailed). "1" means play 1 episode. "SF" means Still Face episode. "Reun." Means reunion episode. "Reac." means reactivity. "Rec." means recovery. "PP BMI" means maternal pre-pregnancy Body Mass Index. "PN" means post-natal. "Intervention" refers to maternal group assignment in prenatal intervention (vs treatment as usual). Note that intercorrelations between covariates are not shown.

***Sex is coded in the standard manner (1=females, 0=males).

**Table 4.** Tests of modification of associations between prenatal maternal stress exposure and infant ANS functioning and temperament by parenting [CCA].

| | RSA Reactivity | | | | | | PEP Reactivity | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | B | P | $R^2$ | $\triangle R^2$ | 95% CI [LL,UL] | | B | p | $R^2$ | $\triangle R^2$ | 95% CI [LL,UL] |
| Poverty | 0.00 | | | | | Poverty | 0.00 | | | | |
| Sex | −0.05 | | | | | Sex | 0.48 | | | | |
| Inter. | 0.29 | | | | | Inter. | 0.54 | ‡ | | | |
| SLE | 0.12 | ‡ | | | | SLE | 0.07 | | | | |
| Sensitivity | 0.22 | | | | | Sensitivity. | −0.19 | | | | |
| PN PSS | −0.16 | | | | | PN PSS | −0.16 | | | | |
| PARxSLE | −0.18 | ** | | | −.31, −0.05 | PARxSLE | −0.13 | ‡ | | | −.26,0.00 |
| Model | | ‡ | 0.28 | 0.15 | | Model | | ‡ | 0.26 | 0.13 | |
| Note: *n*=48 | | | | | | Note: *n*=48 | | | | | |
| **RSA Recovery** | | | | | | **PEP Recovery** | | | | | |
| Poverty | 0.00 | | | | | Poverty | 0.00 | | | | |
| Sex | 0.21 | | | | | Sex | −0.23 | | | | |
| Inter. | 0.04 | | | | | Inter. | −0.09 | | | | |
| SLE | −0.04 | | | | | SLE | −0.09 | | | | |
| Sensitivity | 0.53 | *** | | | | Sensitivity | 0.38 | ** | | | |
| PN PSS | 0.13 | | | | | PN PSS | 0.03 | | | | |
| PARxSLE | 0.14 * | | | | .03, 0.26 | PARxSLE | 0.17 | ** | | | .05, 0.29 |
| Model | | ** | 0.45 | 0.35 | | Model | | ** | 0.40 | 0.30 | |
| Note: *n*=47 | | | | | | Note: *n*=47 | | | | | |
| **Infant Negativity** | | | | | | **Infant Regulation** | | | | | |
| Poverty | 0.00 | ** | | | | Poverty | 0.00 | | | | |
| Sex | 0.37 | ‡ | | | | Sex | 0.09 | | | | |
| Inter. | 0.08 | | | | | Inter. | −0.11 | | | | |
| SLE | −0.04 | | | | | SLE | 0.05 | | | | |
| Sensitivity | −0.17 | ‡ | | | | Sensitivity | 0.19 | ‡ | | | |
| PN PSS | 0.24 ‡ | | | | | PN PSS | −0.28 | * | | | |
| PARxSLE | −0.16 | ** | | | −.25, −.06 | PARxSLE | 0.09 | ‡ | | | −.01, .18 |
| Model | | *** | 0.25 | 0.19 | | Model | | | 0.13 | 0.06 | |
| Note: *n*=99 | | | | | | Note: *n*=99 | | | | | |

‡$p$<.10, * $p$≤.05, ** $p$≤ .01, ***$p$≤ .001 Inter. means intervention. PN means post-natal.

Note: All significant interaction findings remained significant after applying the Benjamini-Hochberg false discovery rate of .05.

Note also that both ANS reactivity and recovery are coded so that larger values reflect increased reactivity and recovery, respectively. Outcomes and sensitivity were standardized to allow comparison across RSA, PEP, and negativity and regulation indices. SLE count was centered.

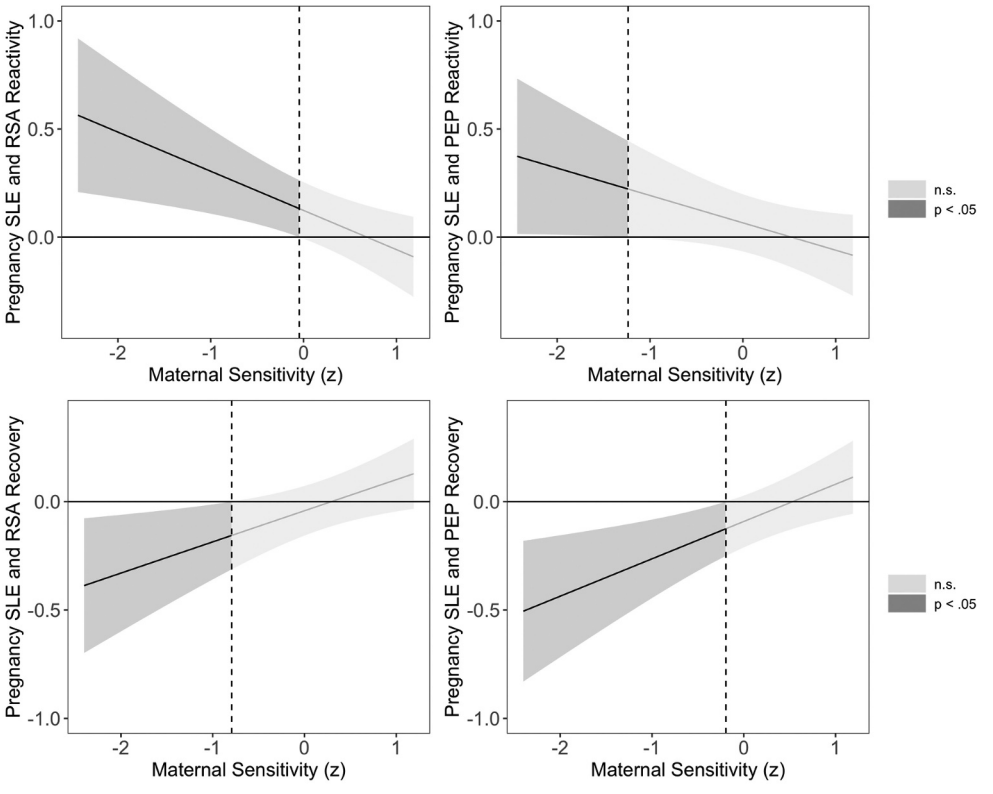


Figure 2. Conditional effect of pregnancy stressful life events and infant ANS outcomes, highlighting regions of significance for parental sensitivity.

with reversed plotting to illustrate how histories of pregnancy stress might modify parenting/child outcome associations (S1 and S3).

### 4.2.1. Predicting RSA reactivity

SLE significantly interacted with sensitivity to predict RSA reactivity. When sensitivity was roughly average or higher, SLE was not associated with RSA reactivity, whereas for below average levels of sensitivity ($z < -.05$) higher SLE was associated with higher RSA reactivity (Figure 2). When plotted differently, at SLE exposure of ~2 events or more, sensitivity predicted lower levels of infant reactivity (S2). Postnatal PSS was not a significant predictor of RSA reactivity.

Simple slopes are plotted using sample Terciles, splitting into three equally sized subgroups, tested at the sensitivity midpoint of the each tercile. * $p < .05$, + $p < .10$.

### 4.2.2. Predicting PEP reactivity

The SLE by sensitivity interaction was similarly patterned to that seen with RSA reactivity, as illustrated by Figure 2, such that SLE predicted greater PEP reactivity at lower levels of sensitivity ($z < -1.25$), but the observed interaction term did not reach significance at the $p < .05$ level ($p = 0.06$). Exploration of simple slopes revealed that SLE was associated at the trend level with lower reactivity at low

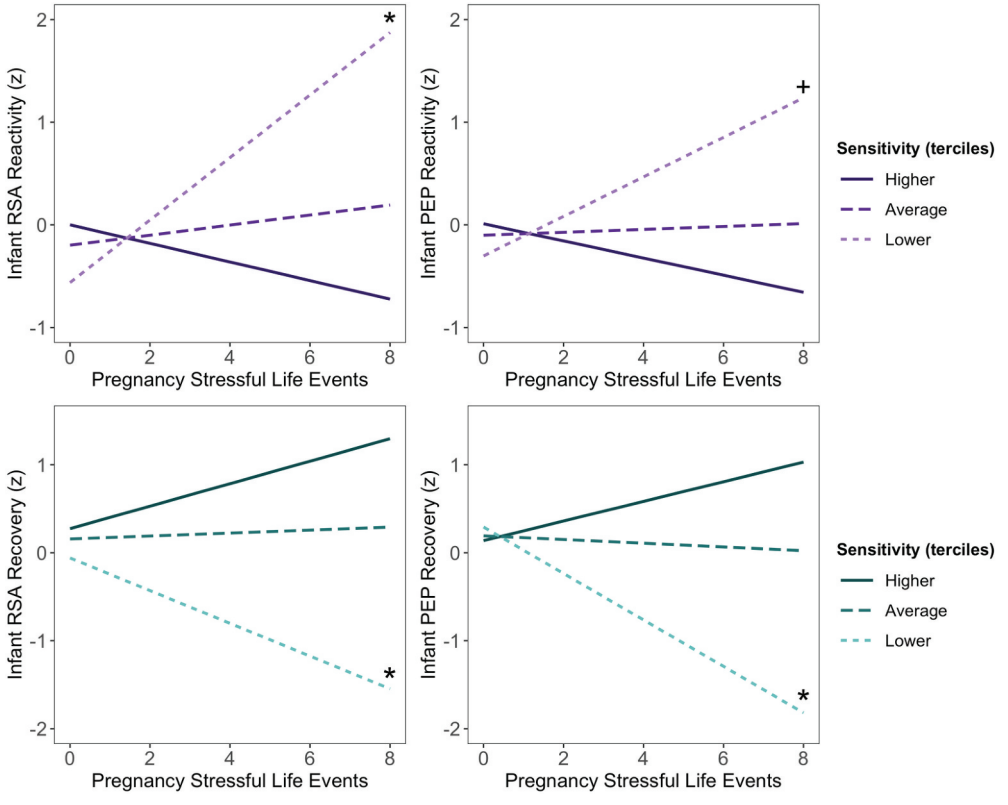


Figure 3. Plots of simple slopes demonstrating estimated associations between pregnancy stressful life events and infant ANS reactivity and recovery outcomes, at various levels of parenting sensitivity.

levels of sensitivity (Figure 3). When plotted differently (when the probe of the interaction was flipped) we note that the interactive association became significant at high levels of SLE (i.e. 4 or higher, $p < .05$; S2). Because the interaction did not reach significance at the $p < .05$, we report main effects – in the full model with interaction and when the interaction was dropped from the model, neither stress nor parenting significantly predicted PEP reactivity. Postnatal PSS was not a significant predictor of PEP reactivity.

### 4.2.3. Predicting RSA recovery

SLE significantly interacted with sensitivity to predict RSA recovery. When sensitivity was average or higher, SLE was not associated with RSA recovery, whereas at lower levels of sensitivity ($z < 0.79$) SLE predicted lower recovery (Figure 2). Plotted differently, sensitivity predicted greater recovery across all levels of SLE exposure (i.e. 1 or more event) (S2). Postnatal PSS was a significant predictor of RSA recovery.

### 4.2.4. Predicting PEP recovery

SLE significantly interacted with sensitivity to predict PEP recovery. When sensitivity was roughly average or higher, SLE was not associated with PEP recovery, whereas at low levels of sensitivity ($z < .19$), higher SLE predicted lower recovery (Figure 2). Plotted

differently, when SLE was ~2 events or more, sensitivity predicted greater recovery (S2). Postnatal PSS was not a significant predictor of PEP recovery.

#### 4.2.5. Predicting temperamental negativity

SLE significantly interacted with sensitivity to predict infant negativity. When sensitivity was roughly average or higher, SLE was not associated with negatively, whereas at lower levels of sensitivity ($z < 1.16$) SLE was positively associated with negativity (e.g. higher SLE was associated with higher negativity). Postnatal PSS was not a significant predictor of temperamental negativity. Covarying for depression did not affect the results although the depression covariate was significantly positively associated with negativity ($t = 2.5$, B = .075, $p = .016$).

#### 4.2.6. Predicting temperamental regulation

The interaction between SLE and regulation did not reach significance ($p = .09$). Examination of the conditional effects of SLE suggested no meaningful associations within our observed data range. Because the interaction was not significant at the $p < .05$ level, we report main effect – in the full model and when the interaction was dropped from the model, sensitivity was significantly positively associated with regulation (e.g. higher sensitivity was associated with higher regulation) (B = .22, $t = 2.197$, $p = .031$). Postnatal PSS predicted lower scores on regulation (B=–.294,$t = -2.052$). When added to the model, depression was negatively associated with regulation (B=–.085,$t = -2.570$, $p = .018$).

#### 4.2.7. Results from the imputed missing data models

Finally, Table 1, S and S3 show that MI results ($N = 154$, 66) are comparable to the CCA (Complete Case Analysis) results presented ($N = 99$, 47). In general, moderation effects were somewhat attenuated but still significant for the same panel of findings observed using CCA for RSA reactivity and recovery, PEP recovery, and Negativity. PEP reactivity effects of the same pattern were trend-level for CCA and MI models.

## 5. Discussion

Limited research indicates that higher prenatal stress may be associated with excessive infant ANS reactivity and a failure to recover from challenge, both of which have been associated with difficulties establishing healthy emotion regulation later in life (Jones-Mason et al., 2018). There is broad agreement in the field of infant mental health that infant psycho-physiological functioning forms within the context of the parent-child or attachment relationship (Larrieu et al., 2019). When the infant experiences sufficient levels of threat, the attachment system is activated and behaviors such as protest are expected. Protest is presumed to terminate upon a sensitive response from the parent (Bowlby, 1969, 1982; Cassidy, 1994). Accordingly, one of the central questions asked in this study was whether the infants of mothers with a history of high prenatal exposure to adverse events showed lower ANS reactivity and/or greater recovery from challenge when their mothers demonstrated higher levels of sensitivity during a paradigm deliberately designed to induce a stress response in infants. Results from this study suggest the answer is yes, and that this is also true for temperamental negativity.

In this study, consistent with extant research, infants showed considerable variability in response but, on average, demonstrated RSA withdrawal during the SF episode (trend-level) and RSA continued to significantly decrease in reunion compared to the play episode (no recovery, continued reactivity). Declining RSA is thought to reflect active attempts by the infant to cope with challenge or stress (Porges, 2007). Given the more limited study of infant PEP, it is notable that sympathetic activity did not differ between play and the SF episode but did significantly decrease between the SF and reunion, also indicating continuing reactivity. Although RSA withdrawal does not always suggest a stress reaction, PEP shortening typically does, and these two measures of ANS activity taken together indicated that at least some children experienced a sustained stress response after the SF episode ended. Similar patterns of ANS findings have been found in populations living in a low-resource and high-stress environments (Jones-Mason et al., 2018).

The main ANS hypotheses of this study were generally supported; sensitivity moderated the association between prenatal stress and ANS during reactivity (PNS significantly, SNS marginally) and recovery (both systems) Maternal prenatal stress exposure was associated with infant PNS and SNS function, with greater exposure predicting more PNS reactivity and less recovery across both systems, but only for infants whose mothers demonstrated lower levels of observed sensitivity. At higher levels of sensitivity, prenatal stressor exposure was unrelated to any ANS outcomes. These results, paired with visual inspection of the patterns of associations (see Figures 1 and 2), suggest a meaningful role for parental sensitivity in infant regulation, across both branches of the infant ANS and for infant behavior. Notably, exploration of the associations for SNS reactivity showed a similar pattern to that of PNS reactivity, revealing that parenting may play a buffering role for the prenatal stress risk effects on both "rest and digest" as well as "fight or flight" response in offspring.

Of note, the results for RSA recovery were more modest than those for other ANS outcomes. Moderation by parenting sensitivity in the prediction of recovery was only detectable at very low levels of sensitivity, suggesting the robust main effect association between parental sensitivity and PNS recovery may be of greater importance for this outcome.

To the best of our knowledge, no other study examines whether parental sensitivity moderates associations between prenatal stress exposures and both PNS *and* SNS, allowing cross-system comparison during this critical early developmental period. Concurrent examination of associations across multiple systems provides a more comprehensive picture of potential ANS effects predicted by prenatal stress exposures, particularly as there is variation in which systems individual children are most responsive to stressors (Rudd et al., 2021).

Prior research, despite differences in prenatal stress and sensitivity measures, is generally consistent with our findings. Recall that, with few exceptions, extant SFP studies examined PNS, and, of those that examined prenatal stress, none included parental sensitivity. For example, our results are fundamentally consistent with Gray et al. (2017) and Suurland et al. (2016) in that higher prenatal stress exposure was associated with lower RSA recovery, again, albeit at lower levels of sensitivity. Though they did not assess parenting sensitivity, our pattern of results align with Suurland et al. (2016), who reported

that infants whose mothers were exposed to greater psychosocial risk showed a continued decrease in PEP in reunion (Suurland et al., 2016).

Although the impact of prenatal stress was not considered, a number of SFP-ANS studies examining the association between sensitivity or related constructs and infant ANS function (Jones-Mason et al., 2018) are worth noting here, as their findings are fairly consistent with our study. For example, studies reported that the infants of sensitive or responsive mothers showed higher PNS activation across the SF and reunion episodes (Bosquet Enlow et al. 2014) and lower HR (Conradt & Ablow, 2010; Moore et al., 2009). Findings in these studies, however, were not without caveats. For example, the PNS results in Bosquet Enlow et al. (2014) were significant only when using a dichotomous sensitivity measure, Conradt and Ablow (2010) reported no significant association between sensitivity and PNS recovery in their final model, and Moore et al. (2009), in contrast to the weight of the SFP literature, found the infants of highly sensitive mothers to have lower PNS in reunion. As noted earlier, the only two SFP studies that examined an SNS measure and sensitivity had smaller sample sizes than the present study and one measured a very different outcome (Ham & Tronick (2009) examined maternal – child physiological synchrony using skin conductance)). In their modified SFP-R study (2 SF and reunion episodes), Bosquet Enlow et al. (2014) reported positive associations between SNS activation (TWA) and maternal insensitivity during both SF episodes, generally consistent with our finding of associations between low sensitivity and greater SNS reactivity (albeit at trend levels).

The present study advances the field in that prenatal stress was found to be consistently associated with infant PNS *and* SNS activity: for PNS reactivity (SNS reactivity at trend levels) and PNS and SNS recovery indices. This unique set of findings, relative to prior literature, is likely because of the novel, simultaneous consideration of prenatal stress exposure, ANS, and parental sensitivity, within an ethically/racially diverse, lower-SES sample. Comparing our results to extant research suggests multiple considerations. For example, one possible explanation for why Suurland et al. (2016) did not find an association between psychosocial maternal risk and PNS reactivity is that the study did not take parenting sensitivity into account. Note that our earlier work (Bush et al., 2017) found no association between SLE and infant negativity, whereas incorporation of parenting in the present study revealed that there was an association for some dyads – depending upon caregiver sensitivity. Moreover, due to the nature of their sample, the mothers from the Suurland et al. sample may not have encountered particularly high levels of stress. Our results may also have been particularly evident due to greater variability in stress exposure in this sample. Accordingly, consideration of the infant-parent relationship is critical, and the effects of stress may be most easily detectable when stress is over a certain threshold.

Bosquet Enlow et al. (2014) reported that findings for parenting main effects on the SNS outcome were more robust than those for the PNS, suggesting that the SNS may be more responsive to changes in parental behaviors. Although our results were significant for PNS and marginal for SNS reactivity, we found that the magnitude of the association between sensitivity and ANS (PNS and SNS) were robust for recovery, which is not necessarily surprising. Most infants are challenged by the SF episodes (Mesman & Emmen, 2013) and most (not all) would be expected to signal parents when distressed (e.g. protest, cry or show other forms

of reactivity). Infants exposed to sensitive parenting, however, have shown quicker recovery than infants who experience insensitive parenting (Jones-Mason et al., 2018). Our findings do suggest that infants whose parents show more sensitive behaviors recover more quickly. It bears emphasizing that greater sensitivity to infant distress is thought to be the key factor in the development of secure attachment (De Wolff & van Ijzendoorn, 1997). The findings on infant temperamental negativity were similar to those of ANS reactivity and recovery. For example, higher levels of prenatal stress exposure predicted greater infant negativity but only at low levels of sensitivity. At higher levels of sensitivity, prenatal stress exposures and infant negativity were either unassociated or, at the highest levels of sensitivity, negatively related. These results also raise the possibility that sensitive parenting may be particularly salient and effective for infants in high-stress environments. Prenatal stress exposures and parenting interactions did not reach significance for temperamental regulation. Sensitivity did have a significant main effect when post-hoc regression analyses were run which is consistent with existing evidence of positive associations between maternal sensitivity (or related concepts) and various self-regulatory constructs (Braungart-Rieker et al., 2010), and provides further suggestion that infants use parents as an external source of regulation.

It is also important to note that patterns of extended reactivity are not necessarily dysfunctional. As attachment theory suggests, patterns of reactivity may be adaptive depending on the environment in which the infant is raised. In fact, extended reactivity may be quite adaptive in a low-resource environment when parents may be distracted by the stresses associated with poverty, and children must prolong protest to achieve proximity. Reactivity that continues unabated, however, may become harmful and, ultimately, may be associated with pathology (Beauchaine, 2015). It is not known if these children will develop some of the negative health outcomes associated with chronic stress activation. Future studies may shed light on this issue.

As referenced earlier, DOHaD theories posit that environmental influences (e.g. nutrition, environmental chemicals, or stress) in utero and in early life can determine health outcomes later in life (Arima & Fukuoka, 2020). One way that early life stress is thought to impact later life health outcomes is through changes in the functioning of physiological systems such as the ANS. The results of this study suggest that sensitive parenting occurring during infancy, a particularly sensitive period of development (Gee & Cohodes, 2021), can moderate the effects of stress on this likely stress-health mechanism. In addition, the findings here enhance empirical support for the babies' use of their parents to regulate themselves during times of stress (Thompson et al., 2019) and that parenting behaviors are associated with the functioning of *multiple* infant regulatory systems, including the PNS and SNS, as early as six months of age. This capacity to observe effects of sensitivity on infant developmental outcomes early in life suggests observation of effects on developmental trajectories and subsequent health outcomes along the entire life span is warranted. Such observations may offer clinicians a chance to identify risk and intervene early in the lives of infants, enhancing effectiveness given the highly plastic nature of the infant brain. Evidence that early life parenting-based interventions may impact ANS function later in life (Tabachnick et al., 2019) is promising in this regard. Overall, our findings support the need to consider the influence of postnatal

rearing factors when theorizing about or examining prenatal programming of child health and wellbeing.

Finally, as stated above, these results support the notion that postnatal parental behaviors may be able to mitigate the potential harm done by maternal prenatal stress. We note, however, that although some studies find long-term consequences associated with exposure to prenatal stress (Douros et al., 2017), a number of studies suggest that at least some of the effects of maternal stress on infant development may dissipate by three years of age or largely fail to appear at all when measured later in life (Liu et al., 2015; Zijlmans et al., 2017). These studies primarily come from countries with highly developed social support systems. It is possible that the provision of support to young families may reduce the stress experienced by parents and thus impact infant health outcomes. Accordingly, we add our voice to those who argue for effective support interventions that target multiple risks facing parents and families.

### *5.1. Limitations and strengths*

The small sample size for analyses of ANS outcomes is a primary limitation, although similar sample sizes are common in this literature (see for review, Jones-Mason et al., 2018), and our analyses with multiple imputation to address missingness strengthened our confidence in the findings. Moreover, significant interactions, with consistent patterning, were detected across the two distinct ANS indices and their calculations, suggesting that models were sufficiently powered, and findings remained after correction for multiple testing. Second, the composite sensitivity scores did not distinguish between different types of sensitive behaviors (i.e. flexibility, sensitivity and engagement). As noted by other researchers (Bosquet Enlow et al., 2014), it is possible that different types of parental behaviors may have different effects on infant functioning. Future studies examining how different types of parental sensitivity influence infant ANS or temperament function may be informative. Another limitation to note is the retrospective recall of stressor exposures, which carries a risk of recall bias. Our specific SLE measure asks about memorable major life events such as divorce, homelessness, incarceration of a partner or themselves, job loss, and critical illness of a close family member, and asks about them during a distinctly memorable period of one's life – pregnancy and the months just prior. Moreover, mothers reported these events within roughly 6 months after the child's birth, a limited amount of time to introduce memory or recall impairment. Arguably, it is unlikely that the mother is going to be unclear about whether she experienced events such as homelessness, jail, or divorce, particularly so proximal to the event. As noted earlier, such measures of events are thought to have limited recall bias and be accurate over a span of years (Krinsley et al., 2003).

The study also had multiple strengths. First, as alluded to above, patterns of response via both the PNS and SNS measures suggest that the SFP did trigger a stress response in some of the children leading to reactivity in the sample on average, although findings revealed different systems were activated in different periods. Second this study, unlike some prior studies, controlled for postnatal maternal stress in all models and depression in temperament models, strengthening the likelihood that prenatal stress exposure may be a relevant factor in the development of ANS outcomes. Third, the study used highly trained post-baccalaureate students and an experienced PhD-level researcher to code the

videotapes to ensure quality parenting data. Fourth, this study used well-validated protocols to elicit and assess infant ANS reactivity.

### 5.2. Recommendations

We have a number of recommendations for the future. First, we used measures to assess parental behavior that were specifically designed for use with the SFP but did not conduct a "global" assessment of sensitivity. More extensive assessments of parental sensitivity such as, for example, that provided by the Q-sort procedure (Pederson & Moran, 1995), may be ideal for use in future analyses of infant ANS and sensitivity. Second, carefully controlled longitudinal studies with diverse samples experiencing a range of adversities are critical. Our findings suggest that parental sensitivity is especially important for future health among populations experiencing higher levels of adversity, however, this requires further longitudinal confirmation. Third, temperament or physiology may act as a proxy for environmental sensitivity consistent with the differential susceptibility hypothesis (Burgess et al., 2003; Bush & Boyce, 2016). Future research might look at whether the differences in temperament and ANS reactivity found here may confer differential susceptibility to later environmental effects. Fourth, although our sample size precluded analysis of the simultaneous coordination of PNS and SNS data, such multisystem studies able to model the coordination or lack thereof across those systems will be valuable, particularly those that include other systems such as the HPA axis. Moreover, such studies will advance understanding of the influence of and the relationship between the different major components of the stress response (Rash et al., 2016). Fifth, because fetal development changes dramatically throughout pregnancy more research is needed examining the impact of the timing and chronicity of stress exposure (Jelicic et al., 2022; Scheinost et al., 2017). Sixth, although there is great interest in sex-specific effects of prenatal stress on offspring, few studies report sex differences in infant ANS function (Jones-Mason et al., 2018), and the literature is mixed with respect to sex-specific effects of prenatal stress on offspring in general (Rudd et al., 2022; Sutherland & Brunwasser, 2018). Thus, moderation by child sex is of potential value for future investigations. Finally, most prenatal stress research focuses on the mother. Future research should examine the role of the history of stress exposures experienced by fathers/partners and what, if any, association, exists with offspring outcomes.

## 6. Conclusion

This study provides one of the earliest demonstrations of associations between prenatal stress exposures, parenting, and infant stress reactivity and recovery. Perhaps, the most important message of this study is, however, that babies born to women who have experienced adversity during pregnancy are not destined to experience physiological dysfunction and illness, as effects are heterogeneous and may be buffered by a range of other factors. Future longitudinal studies extending this research to health outcomes are critical for determining whether parenting may help to protect offspring in this manner. Moreover, if sensitivity does provide a buffer against prenatal adversity, then

interventions should be designed to create environments that protect children *and support parents* (Sanders et al., 2021; Waters et al., 2018). Relatedly, although the infant experiences the world through the parent and the influence of the parents on developmental trajectories is profound, the family, nevertheless, exists in a larger social context that too often includes damaging and disempowering structural inequalities. A large and growing literature has developed demonstrating that these structural inequalities impact social and health disparities experienced by parents (Cockerham, 2013) and particularly parents of color (Conradt et al., 2020). In this way, the infant also experiences disparities. Ultimately, to support children's wellbeing and health, support must extend to the entire family and community (Bowlby, 1969, 1982).

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## Disclosure statement

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