Published in final edited form as:

Dev Psychobiol. 2015 December ; 57(8): 961–973. doi:10.1002/dev.21328.

Effects of Prenatal Factors and Temperament on Infant Cortisol Regulation in Low-Income Mexican American Families

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Abstract

Prenatal psychosocial exposures can significantly affect infant health and development. Infants with higher temperamental negativity are theorized to be more susceptible to environmental exposures. We evaluated the interaction of prenatal maternal exposures and infant temperamental negativity to predict infant cortisol response to mildly challenging mother-infant interaction tasks. Participants included 322 Mexican American mother-infant dyads (mother age 18–42; 82% Spanish-speaking; modal family income \$10,000–\$15,000). Mothers reported depressive symptoms and social support prenatally and infant temperamental negativity at 6 weeks postpartum. Salivary cortisol was collected from infants before and after mother-infant interaction tasks at 12 weeks. Higher prenatal maternal depressive symptoms and lower social support predicted higher cortisol among infants with higher temperamental negativity. Higher infant temperamental negativity predicted an increase in maternal distress and a decrease in social support from prenatal to 12 weeks postpartum. Interactive influences of maternal social-contextual factors and infant temperament may influence the development of infant neurobiological regulation and promote or strain maternal and infant adaptation over time.

Keywords

prenatal depression; temperament; cortisol; social support

INTRODUCTION

The prenatal environment has received increasing interest as a contributor to child developmental and health outcomes in high risk populations. The prenatal programming hypothesis describes the process of fetal adaptation to the intrauterine environment, contending that maternal exposures during pregnancy affect the intrauterine environment in a manner which affects fetal and infant growth, brain development, and physical and developmental health (Talge, Neal, & Glover, 2007). The prenatal period has been conceptualized as a sensitive period in which suboptimal fetal environments increase the risk of low birth weight and poor birth outcomes, and contribute to long-term risks of obesity, cardiometabolic disorders, and other diseases later in life (Fernandez-Twinn & Ozanne,

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Conflicts of Interest: The authors have no conflicts of interest, financial or otherwise.

2006; Reynolds, 2013; Talge et al., 2007). Although behavioral exposures such as alcohol or smoking are more commonly studied, maternal prenatal stress and depression also can affect infants. Maternal prenatal depression has been linked to a broad range of adverse infant and child health and developmental outcomes, including low birth weight, pre-term birth, delayed motor, and cognitive development, behavioral and emotional problems, and poor physical health (Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003; DiPietro, Novak, Costigan, Atella, & Reusing, 2006; Field, 2011; Lester, Marsit, Conratt, Bromer, & Padbury, 2012).

Goodman (2007) provides a framework suggesting that prenatal depression impairs the development of infant biological neuroregulatory systems, predisposing children to behavioral and emotional problems. The impact of maternal prenatal distress on infants may be partly due to effects on the developing hypothalamic-pituitary-adrenal (HPA) axis. A primary pathway of the stress response system, the HPA regulates the production and release of the glucocorticoid hormone cortisol. Maternal prenatal stress may interfere in the normal development of the HPA axis, disrupting subsequent capacities for physiological and behavioral regulation, and increasing long-term risk of behavioral and physical disorders (Glover, 2015; Pervanidou & Chrousos, 2012; Talge et al., 2007; Weinstock, 2005). One route for these effects may be via fetal exposure to elevated maternal cortisol, which has been associated with infant HPA stress responses and developmental impairments (O'Connor, Bergman, Sarkar, & Glover, 2013; Sandman, Davis, Buss, & Glynn, 2012).

Dysregulated HPA activity can be evident in the form of exaggerated or attenuated reactivity, higher or lower basal levels, or flattened diurnal slopes (Gunnar & Vazquez, 2001; Miller, Chen, & Zhou, 2007), and both exaggerated and attenuated cortisol activity are associated with behavioral and physical health problems later in life (Shirtcliff, Peres, Dismukes, Lee, & Phan, 2014). Animal models primarily link prenatal stress with elevated responsiveness of the offspring HPA axis, while results with human children are more variable (Fowden, Giussani, & Forhead, 2005; Matthews, 2002). For example, elevated maternal cortisol in pregnancy predicted higher infant cortisol response to a heel stick at birth (Davis, Glynn, Waffarn, & Sandman, 2011). O'Connor et al. (2013) reported that 17-month infants exposed to high cortisol in utero had elevated pre-stress cortisol levels but blunted response across a separation-reunion stressor. Higher prenatal maternal depression, which may be associated with elevated maternal cortisol, has been theorized to program heightened HPA reactivity in the infant, while lower prenatal depression may result in a less reactive infant (Field, Diego, & Hernandez-Reif, 2006; Sohr-Preston & Scaramella, 2006). Higher prenatal depression has been shown to predict elevated ACTH (a precursor to cortisol) in cord blood of neonates (Marcus et al., 2011), higher diurnal cortisol levels in 5 year old children (Gutteling, de Weerth, & Buitelaar, 2005) and higher cortisol reactivity to social stress in young adulthood (Entringer, Kumsta, Hellhammer, Wadhwa, & Wust, 2009).

The current study evaluates a prenatal programming model in a sample at high risk of prenatal depression. Low income and ethnic minority women experience significantly elevated rates of perinatal stress and depression relative to middle-income Caucasian women (CDC, 2008; Heilemann, Frutos, Lee, & Kury, 2004), putting their children at higher risk of developmental and health problems. Hispanic children are more than twice as likely to be

raised in poverty as non-Hispanic white children (37% vs. 16%; Addy, Engelhardt, & Skinner, 2013). Hispanic children in low-income families face significant physical and mental health disparities evident early in life, including developmental, behavioral, and cognitive deficiencies, overweight/obesity, and physical health complaints (Flores, 2010; Fuller et al., 2009). Distress experienced by Mexican American mothers during pregnancy may be one contributor to poor health outcomes for their children. Contextual adversities endemic in the lives of poor Mexican American families may become embedded in developing systems of child biological regulation, contributing to health disparities over the life course.

However, despite the presence of elevated prenatal risk, infants born to Mexican-origin women have unexpectedly favorable birth outcomes (D'Anna-Hernandez, Hoffman, Zerbe, Coussons-Read, Ross & Laudenslager, 2012; Fuentes-Afflick & Lurie, 1997; Fuller et al., 2009), which may provide a degree of protection from later health problems. For some women and their infants, the presence of protective factors in the prenatal period may compensate for elevated risk. Social support during pregnancy is one such protective factor that has been linked to a number of beneficial outcomes, including healthier maternal pregnancy behaviors, fewer birth complications, higher birth weight, and reduced distress to novelty among six to eight week infants (Campos et al., 2008; Feldman, Dunkel-Schetter, Sandman, & Wadhwa, 2000). Mexican American cultural values may heighten the role that prenatal social support plays as a protective resource, as the relation between prenatal social support and stress has been found to be stronger among Latina women than non-Hispanic women (Campos et al., 2008). McGlade, Saha, and Dahlstrom (2004) describe an “informal system” of intergenerational and neighborhood social support within Latino communities that collectively provides protection for pregnant women. In low income Mexican–American families, core cultural values related to family and kinship support for pregnant women may enhance the protective effects of social support on fetal and infant development (Bender & Castro, 2000; Diaz, Le, Cooper, & Muñoz, 2007). Latina mothers' reports of prenatal social support predict superior psychosocial adjustment across the perinatal period, better infant birth outcomes (Collins, Dunkel-Schetter, Lobel, & Scrimshaw, 1993; Martinez-Schallmoser, Telleen, & MacMullen, 2003), and lower cortisol reactivity (Luecken et al., 2013).

Infant temperament, defined as early constitutionally-based differences in infant reactivity and regulation (Rothbart & Derryberry, 1991), has also been associated with long-term developmental outcomes. Temperament is presumed to be a biologically-based trait, and individual differences in temperament are apparent in newborns and remain relatively stable across development (Compas, Connor-Smith, & Jaser, 2004; Rothbart, 2007; van IJzendoorn & Bakermans-Kranenburg, 2012). Temperamental negativity, which encompasses fear, anger-frustration, and social discomfort in the infant (Rothbart, 2007), has been identified as a potent risk factor for infant and child dysregulation (Compas et al., 2004; Dougherty, Klein, Olino, Dyson, & Rose, 2009). Temperamental negativity is characterized by a tendency to experience heightened arousal, making children more reactive to environmental or social conditions. Prenatal depression has been found to predict higher negative infant temperament (Buitelaar et al., 2003; Huizink, De Medina, Mulder, Visser, & Buitelaar, 2002). Further, infant temperamental negativity can challenge maternal functioning and

increase postpartum depression (Britton, 2011), suggesting that the link between maternal distress and infant negative affectivity is bidirectional. Higher infant negativity may increase maternal depression and decrease a new mother's social support in the postpartum period, thereby increasing the potential health risks to the infant.

Traditionally, temperamentally reactive children are considered at elevated risk for behavioral maladjustment, particularly if exposed to a stressful or low supportive environment. A diathesis-stress framework for understanding the impact of temperamental negativity on child outcomes views temperamental negativity as a vulnerability factor, increasing the risk for poor outcomes in risky environments. For example, hostile parenting styles may exert a stronger negative influence on socioemotional adjustment among children high in negative affectivity than less vulnerable children (Morris et al., 2002; Park, Belsky, Putnam, & Crnic, 1997). Recently, theorists have advanced an alternative view, in which negative temperament indicates heightened sensitivity to negative as well as positive environments. Rather than viewing infants with temperamental negativity as *vulnerable*, Belsky's (2007) model, for example, views negative temperament as a susceptibility factor, increasing the impact of negative exposures but also enabling infants to benefit disproportionately from supportive environments. The related theory of vantage sensitivity (Pluess & Belsky, 2013) focuses on variability in the consequences of exposure to positive environments as a function of characteristics endogenous to the child, such as temperament, genetic makeup, biological reactivity, or personality traits. For example, infants with higher negative emotionality may be more effective at eliciting caregiver support than "easy" infants (van IJzendoorn & Bakermans-Kranenburg, 2012). In support of these theories, Kochanska, Aksan, and Joy (2007) reported that supportive parenting had stronger effects on self-regulation for children higher on temperamental negativity.

The current study evaluates an integrative model of prenatal programming and differential susceptibility, suggesting that infants higher on negative temperament may be more susceptible to both positive (supportive) and negative (depressive) maternal prenatal experiences. Theories of differential susceptibility have rarely been extended to encompass the prenatal environment. In an exception, Babineau et al. (2014) recently demonstrated a differential susceptibility effect in which prenatal maternal depression interacted with genetic susceptibility (5-HTTLPR genotype) to predict mother-rated dysregulation in 3–6 month old infants. Infants with susceptible genotypes demonstrated higher dysregulation after exposure to maternal prenatal depression, but less dysregulation when prenatal depression was low. Like postpartum exposures, a risky prenatal environment may interact with biological susceptibility to influence infant development. It is not known if infants with negative temperament are disproportionately affected by negative or positive maternal prenatal experiences.

The current study contributes to research on prenatal programming as well as risk and protective influences on Mexican American children's health. Although it is widely recognized that prenatal and early life factors can set the stage for lifespan health, few studies have been conducted with low income Mexican American women and their infants, yet the effects of prenatal exposures have been shown to differ among socioeconomic and ethnic groups (Field et al., 2006). In low-income Mexican–American families, high risks

associated with poverty, elevated prenatal distress, and immigrant status, as well as strong cultural values of social support for pregnant women, provide a powerful context for investigation of positive and negative prenatal influences on infant HPA activity. The current study evaluated the interactive influences of prenatal depressive symptoms, prenatal social support, and 6 week infant temperamental negativity on infant cortisol reactivity at 12 weeks of age in a sample of very low-income Mexican American women and infants. We hypothesized that temperamental negativity would predict elevated cortisol among 12-week infants whose mothers reported higher prenatal depression, but lower cortisol among infants whose mothers reported higher social support. We also investigated the bidirectional relations of maternal distress, social support, and infant negative temperament, hypothesizing that women with more temperamentally negative infants would show increases in depression and decreases in social support at 12 weeks postpartum.

METHODS

Participants

Participants included 322 women (mean age=27.8, SD=6.5, range 18–42) and their infants. Data for the analyses were collected at four time points: prenatal (26–38 weeks gestation; mean 35.4 weeks, SD=2.8) and 6, 9, and 12 weeks postpartum. Women were recruited from a hospital-based prenatal clinic that serves low-income women from the surrounding community. Eligibility criteria included: 1) self-identification as Mexican or Mexican American, (2) fluency in English or Spanish, (3) age 18 or older, (4) low-income status (family income below \$25,000 or eligibility for Medicaid or Federal Emergency Services coverage for the birth), (5) no prenatal evidence of a serious infant health or developmental problem, and (6) delivery of a singlet baby. Eighty-six percent were born in Mexico (14% U.S. born), and 82% primarily spoke Spanish. See Table 1 for additional demographic characteristics.

Procedure

During prenatal care appointments, women were approached by a female, bilingual interviewer who explained the study and assessed eligibility. Of women who were eligible, 56% agreed to a prenatal home visit during which informed consent was obtained. To minimize participant burden, the study followed a “planned missingness” design (Enders, 2010): all participants were assigned to complete the 6 week visit, but a random 2/3 of the sample were assigned to complete the 12 week visit. Women who did not complete the 12 week home visit completed a brief phone survey instead to assess depressive symptoms. Random assignment to planned missingness groups was determined by a computer algorithm prior to the first data collection. Of the 322 women who consented to the study at the prenatal visit, 312 (97%) completed the 6 week visit, and 205 (95%) completed the 12-week visit.

Interviews were conducted at participants' homes in their choice of Spanish (82%) or English (18%). Due to variability in literacy, informed consent and survey questions were read aloud, and women were given written and graphic descriptions of survey item response formats. Postpartum interviews were scheduled within one week of the infant's

chronological age, but for infants born at less than 37 weeks gestation, the interview was conducted at their corrected age. At the 12 week interviews, salivary cortisol samples were collected from mothers and infants before and after video-recorded mother-infant interaction tasks that began approximately 30 min after arrival in the home. Interviews were scheduled at the mother's convenience; between 8:00 AM and 4:30 PM (median 11:30 AM; total duration approximately 2 hr). Women were compensated with \$75 and small gifts (e.g., bath oils) at the prenatal interview, and \$50 and small gifts (e.g., bibs, bath toys) at the 6 and 12 week interviews. The study was approved by the Internal Review Board at Arizona State University and carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Mother-infant interaction task—To provide a context for cortisol sampling, a series of five structured, video-recorded mother-infant tasks were conducted at the 12 week home visit. Mother-infant interaction tasks capture a primary, ecologically valid context for eliciting infant reactivity. The tasks were based on widely-used, well-characterized, manualized components (e.g., an anger/frustration eliciting task and the peek-a-boo task from the Lab-TAB (Goldsmith & Rothbart, 1993) and Bayley Scales of Infant Development II (BSID-II; Bayley, 1993), designed to minimize variation that might be attributable to maternal differences. The infant was in an infant seat with the mother seated directly across from him/her. The episodes included 1) Free play (5 min), 2) Arm Restraint (Lab-TAB; an anger/frustration eliciting task; 2 min), 3) Soothing (3 min), 4) Teaching task (BSID-II; frustration eliciting task; 5 min; mothers are asked to “teach” her child a task from the that reflects a skill 1–2 months beyond the infant's capabilities), and 5) Peek-a-boo (Lab-TAB; standardized; 3 min).

Measures

Depressive symptoms—The 10-item Edinburgh Postnatal Depression Scale (Cox, Holden, & Sagovsky, 1987) was completed by the mother prenatally and at 9 and 12 weeks postpartum (prenatal $\alpha=.86$; 9 week $\alpha=.84$). The EPDS has been validated in English (Cox et al.) and Spanish (Garcia-Esteve, Ascaso, Ojuel, & Navarro, 2003). An error in response sets led to one item (“You have been so unhappy that you have been crying”) on the prenatal measure being treated as missing data for 99 participants. Multiple imputation (Mplus 7; Muthén & Muthén, 2012) was used to impute missing item-level values for these participants (Reiter & Raghunathan, 2007). Responses were summed and higher scores reflect higher depressive symptomatology.

Prenatal social support—The 17-item *MOS Social Support Survey* (Sherbourne & Stewart, 1991) assessed emotional and tangible support at the prenatal visit ($\alpha=.96$) and at 12-weeks postpartum ($\alpha=.96$). Participants rated how often different kinds of support are available to them if they need it (e.g., “Someone who shows you love and affection”). Response choices ranged from “0=Never” to “4=All of the time”. Higher scores indicate higher support.

Temperamental negativity—Maternal ratings of infant temperament were obtained at the 6-week visit using the negativity subscale of the Infant Behavior Questionnaire-Revised

(IBQ-R; Gartstein & Rothbart, 2003; $\alpha=.61$). Higher scores reflect higher temperamental negativity.

Control variables—Infant cortisol levels can be influenced by a wide range of contextual factors such as time of day, infant feeding time, infant waking time, and breastfeeding status. These variables are not expected to explain relations between the independent variables (IV) and the dependent variable (DV), but were considered analytically as covariates. Because they are not in a causal pathway with the DV, controlling for covariates is not necessary but can increase efficiency in estimation (Sauer, Brookhart, Roy, & Vanderweele, 2013). In contrast, confounding variables are associated with both the IV and the DV, and can potentially change or explain the relations between them (MacKinnon & Luecken, 2008). Potential confounds included: socioeconomic status (household income, maternal education) and postpartum maternal depression, social support, or maternal cortisol. Potential covariates and confounds were evaluated theoretically and empirically. Variables identified in prior research as predictive of cortisol and statistically related to maternal support, depression, and/or infant cortisol in the current analyses were included in final models.

To address possible negativity bias in mother reports of infant temperamental negativity at 6 weeks postpartum, maternal negative mood state at 6 weeks was assessed with five items from the Positive and Negative Affect Scale (PANAS; Watson & Clark, 1994): nervous, upset, hostile, irritable, ashamed. Women rated each mood from 1=“not at all” to 10=“very much so”. Item ratings were summed to create a negative mood score. Maternal acculturation was assessed as a potential covariate with the Acculturation Rating Scale for Mexican Americans (ARSMA II; Cuellar, Arnold, & Maldonado, 1995), a 30-item scale focused on language and ethnic affiliation patterns. Other potential covariates included maternal country of origin (Mexico or US), breastfeeding status at 12 weeks (coded 0=bottle-feeding, 1=partial or exclusive breastfeeding), and delivery and birth outcomes (delivery type, gestational age, birthweight, APGAR score, birth difficulties) obtained from medical records at the hospital of birth.

Infant cortisol—Saliva samples were obtained from infants and mothers at the 12-week home visit. Samples were collected immediately prior to the first task (T0), and at 0 (T1), 20 (T2), and 40 (T3) minutes after all the mother-infant tasks were complete, using Salivette (mothers) and Sorbette (infants) sampling devices (Sarstedt, Rommelsdorf, Germany; Salimetrics Inc, State College, PA). Oral stimulants were not used, and mothers were asked not to feed the baby for 30 minutes prior to or during the task. Saliva samples were frozen and mailed to Salimetrics Inc where they were assayed for free cortisol. Area under the curve with respect to ground (AUCg) was calculated to capture total infant cortisol response to the tasks. AUCg was chosen over other measures of cortisol response because it captures both sensitivity and intensity of response (Fekedulegn et al., 2007), the amount of time between the samples was not identical (as can happen when sampling in the home environment), and preliminary analyses did not show significant reactivity (increase from baseline) to the task ($p=.38$). We calculated AUCg for participants with at least 3 of 4 viable cortisol samples. AUCg was log-transformed to correct for deviations from normality. Five

infants with cortisol values >4 SD from the sample mean were removed a priori from analyses.

Data Analyses

Analyses were conducted using the general analysis program MPlus 7 (Muthén & Muthén, 2012) because of its capability for full information maximum likelihood (FIML) estimation, ideal for the planned missing data design of the study (Enders, 2010). Infant cortisol AUCg was the DV. Prenatal depressive symptoms, prenatal social support, and infant temperament were IVs. The first model included maternal depressive symptoms, temperamental negativity, and the interaction of depressive symptoms and negativity in the prediction of infant cortisol AUCg. The second model evaluated maternal social support, temperamental negativity, and the interaction of social support and negativity in the prediction of infant cortisol AUCg. In all models, IVs were treated as continuous variables, centered at the sample mean. Because controlling for covariates can yield biased estimates of the impact of an IV on a DV (Jaccard, Guilama-Ramos, Johansson, & Bouris, 2006), we took a conservative approach by analyzing models both with and without covariates. Potential outliers were identified by examination of Mahalanobis distance, studentized residuals, and Cook's D. Primary analyses were repeated after removing outliers.

Additional regression analyses were conducted to evaluate the longitudinal prediction of maternal depression and social support 12 weeks postpartum by temperamental negativity. Depressive symptoms at 12 weeks were predicted from prenatal depression and infant temperamental negativity. Similarly, social support at 12 weeks was predicted by prenatal social support and infant temperamental negativity.

RESULTS

Preliminary Analyses

Correlations between study variables are shown in Table 2. Infant sex, gestational age, birth weight, premature or low birth weight status, birth difficulties, delivery type, household income, maternal education, maternal acculturation, maternal age, maternal smoking status (current or history), maternal BMI, timing of prenatal assessment, time of last infant feeding, and breastfeeding status were not significantly associated with maternal depression, social support, temperamental negativity, or infant cortisol. Maternal country of birth was associated with infant temperamental negativity such that women born in Mexico reported lower infant negativity than women born in the US ($p < .01$), but had no significant relations to maternal depressive symptoms, social support, or infant cortisol. Time of day and mother's AUCg at 12 weeks were significantly correlated with infant cortisol. Therefore, time of day and mother's 12 week AUCg were selected as covariates for final models. Final models also included postpartum maternal depressive symptoms or social support to adjust for the infant's current environmental exposure, and maternal negative mood at 6 weeks postpartum to adjust for potential negativity bias in ratings of infant temperamental negativity.

In the model with depressive symptoms as an IV, three cases were identified as potentially influential. For models with social support as an IV, one potential outlier was identified.¹

Primary Analyses

Prenatal depressive symptoms and infant temperamental negativity—Infant cortisol response to the mother-infant interaction task at 12 weeks postpartum was first predicted from prenatal depressive symptoms, infant temperamental negativity, and their interaction. This model did not adjust for any covariates. The interaction term was statistically significant, unstandardized estimate=.014, SE=.006, 95% CI [.003, .025], $p=.016$ (see Fig. 1). Higher prenatal maternal depressive symptoms were associated with higher cortisol AUCg among infants with higher temperamental negativity but lower cortisol AUCg among infants with low temperamental negativity. After adjustment for time of day and postpartum maternal AUCg, mood, and depressive symptoms, unstandardized estimate for the interaction=.012, SE=.006, 95% CI [.001, .023], $p=.034$. When analyses were repeated with the three potentially influential cases removed, the unstandardized estimate for the interaction=.019, SE=.007, 95% CI [.005, .033], $p=.008$.

Prenatal social support and infant temperamental negativity—Next, infant cortisol AUCg was predicted by prenatal social support, infant temperamental negativity, and their interaction. The interaction term was statistically significant, unstandardized estimate=-.039, SE=.018, 95% CI [-.074, -.003], $p=.033$ (see Fig. 2). Low social support prenatally was associated with higher infant cortisol among infants with high temperamental negativity but lower cortisol among infants with low negativity. After adjusting for time of day and postpartum maternal mood, maternal AUCg, and maternal social support, the unstandardized estimate for the interaction=-.033, SE=.017, 95% CI [-.068, .001], $p=.054$. When analyses were repeated adjusting for covariates but removing the potentially influential case, the unstandardized estimate for the interaction=-.046, SE=.021, 95% CI [-.087, -.005], $p=.028$.

Postpartum maternal depressive symptoms and social support

Higher temperamental negativity at 6 weeks predicted increased maternal depressive symptoms at 12 weeks, adjusting for prenatal depressive symptoms (unstandardized $\beta=1.12$, $t(297)=3.29$, $p=.001$; model $R^2=.18$). Similarly, higher temperamental negativity predicted decreased maternal social support at 12 weeks, adjusted for prenatal social support (unstandardized $\beta=-2.78$, $t(194)=-2.36$, $p=.019$; model $R^2=.46$).

DISCUSSION

Risks to fetal and infant development associated with prenatal stress may be exacerbated in low-income ethnic minority families, who often face physical, emotional, social, and financial stressors during the perinatal period (Bloom, Glass, Curry, Hernandez, & Houck,

¹For analyses of depressive symptoms, the first case had the highest rated infant negativity and no prenatal depressive symptoms. The second had mean level infant negativity but the highest reported maternal depressive symptoms. The third had infant negativity 3 SD above the mean and maternal depressive symptoms 2 SD above the mean. This participant also reported very low social support (>2 SD below the mean) and was also identified as a potential outlier for analyses with social support.

2013; Dominguez, Dunkel Schetter, Glynn, Hobel, & Sandman, 2008). The development of biological stress response systems is a plausible mechanism through which maternal distress during pregnancy may affect infant health. Maternal distress may moderate the development of the fetal HPA axis, resulting in dysregulations associated with subsequent behavioral and health problems (Reynolds, 2013; Lester et al., 2012), while supportive environments may promote better infant health and development. However, recent theories of differential susceptibility and vantage sensitivity posit that genetic or constitutionally based traits such as reactive temperament render children disproportionately susceptible to both positive and negative aspects of the environment (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Pluess & Belsky, 2013).

In a sample of low-income Mexican-American women and infants, we evaluated the interactions of prenatal depressive symptoms and social support with infant temperamental negativity to predict infant cortisol output across mildly challenging mother-infant interactions. Higher prenatal maternal depressive symptoms predicted elevated cortisol among 12-week infants with higher temperamental negativity, but lower cortisol among infants with low temperamental negativity. For infants of mothers reporting few depressive symptoms, temperament did not predict cortisol AUCg. Prenatal social support interacted with temperamental negativity in a similar manner to predict infant cortisol at 12 weeks: lower social support predicted higher cortisol for infants with high temperamental negativity, but there was little difference in cortisol among infants whose mothers reported high social support. Results remained statistically significant after adjusting for relevant covariates including postnatal depressive symptoms and social support, suggesting that the effects were more strongly associated with the prenatal environment than the current environment.

Our results suggest that the impact of infant temperamental negativity on later cortisol response is affected by the prenatal psychosocial environment. Temperamental negativity was associated with higher infant cortisol at high levels of prenatal depressive symptoms or low levels of prenatal social support. However, a more supportive prenatal environment did not affect infants with high temperamental negativity more than infants with low temperamental negativity. Overall, our results do not appear to support a differential susceptibility model of the impact of the prenatal environment on infant cortisol. First, the significant relation of prenatal depressive symptoms to infant temperamental negativity does not fulfill the criteria of independence between the susceptibility factor and the environmental factor (Belsky et al., 2007). Second, although prenatal support did not predict temperament, infants higher on temperamental negativity were not more affected by a positive environment (high social support) than infants low on temperamental negativity. Although the interpretation of a cortisol response is complex, in the current analyses, infant negative emotionality appears to have functioned as a vulnerability factor, increasing the impact of exposure to prenatal depression and low social support on later cortisol output. The impact of a positive prenatal environment was consistent across levels of temperamental negativity. In addition, we found evidence of a contrasting effect of high depressive symptoms or low support for infants low on negativity.

The lack of support for differential susceptibility may be related to our focus on the prenatal environment. Existing tests of differential susceptibility and related theories focus on

postpartum or early life environmental exposures. To our knowledge, Babineau et al. (2014) is the only other study to evaluate differential susceptibility to the prenatal environment. Babineau et al. evaluated the interaction of prenatal depression and a genetic susceptibility factor (5-HTTLPR) on mother-reported child behavioral/emotional dysregulation, and did not evaluate the impact of a positive prenatal environment. Our study is unique in the inclusion of an objective outcome measure of infant dysregulation (cortisol response to a mother-infant task), and temperamental negativity as the susceptibility factor. Despite these differences, both studies found that exposure to maternal prenatal depression had a stronger effect on infant dysregulation for infants higher on the susceptibility factor. The studies differ, however, in the impact of prenatal depression on infants low on the susceptibility factor – Babineau et al. found no effect of prenatal depression, while we found a contrasting effect. This unique context of ethnic minority status, chronic stress, and low resource availability in the current sample may have contributed to differences in study outcomes.

Differential susceptibility theories focus on those with high sensitivity, with the assumption that environmental factors have little or no impact on individuals low on the susceptibility factor. Yet in our study, a negative prenatal environment was associated with lower cortisol than a positive prenatal environment for infants with low negativity. Temperamentally “easy” infants may fail to elicit caregiving attention from a distressed mother, while temperamentally “difficult” infants may elicit harsh responses (van IJzenboorn & Bakermans-Kranenburg, 2012). Our data indicate that a negative prenatal environment can result in heightened or blunted cortisol, depending on temperament. Evolutionary theory suggests that prenatal programming may be adaptive by preparing infants for idiosyncratic characteristics of the postnatal environment (Kapoor, Dunn, Kostaki, Andrews, & Matthews, 2006). Maternal distress during pregnancy may signal a harsh environment for the infant upon birth, and prenatal programming that alters fetal development to perform optimally in a harsh environment may be adaptive. From a survival standpoint, a healthy response to stress typically involves some degree of reactivity. However, attenuated cortisol may assist infants in a stressful environment by limiting HPA responses that could be biologically damaging during a sensitive period of development, while heightened reactivity may increase alertness to an unpredictable and risky environment. However, across time and development, these patterns of reactivity may be less adaptive. Attenuated cortisol may reflect failure of the infant's HPA axis to initiate an adequate response, which could impair the critical development of self-regulatory abilities. Attenuated cortisol, reported in a number of studies evaluating the neuroendocrine impact of early life adversity (Gunnar & Vazquez, 2001), has been linked to externalizing problems in childhood and late adolescence (Hagan, Roubinov, Mistler, & Luecken, 2014; Murray-Close, Han, Cicchetti, Crick, & Rogosch, 2008). Both exaggerated and blunted HPA axis activity are linked to mental and physical health problems (Shirtcliff et al., 2014). Our results suggest that a negative prenatal environment may have maladaptive effects for infants on either extreme of temperamental negativity. Future studies may want to evaluate non-linear models that consider potential benefits of moderate levels of temperamental negative affectivity early in life.

In our sample, higher prenatal depressive symptoms predicted higher infant temperamental negativity at 6 weeks. Further, new mothers of infants with higher temperamental negativity reported an increase in depressive symptoms and a decrease in social support from the

prenatal period to 12 weeks postpartum, suggesting that infant temperament may affect the postpartum environment in a manner that increases risk. The reciprocal relations of maternal depressive symptoms and infant temperamental negativity found in the current study are supported by previous theory and empirical studies. The relation of maternal prenatal depression to infant temperamental negativity may reflect inherited predispositions to negative affect, prenatal programming, or shared method variance (Compas et al., 2004). Although not predicted by prenatal social support, higher infant temperamental negativity at 6 weeks predicted decreased social support at 12 weeks postpartum, adjusting for prenatal support. Infants with negative temperament and a dysregulated HPA axis may be at elevated risk of future mental health problems, particularly if exposed to continuing postnatal adversity (Lester et al., 2012). Experiences with an irritable infant may increase maternal risk of postpartum depression and decrease the availability of support, potentially compounding future risks for mother and infant.

There are several potential mechanisms by which the prenatal psychosocial environment could impact developing infant neurobiological activity. Stress that increases prenatal maternal cortisol could directly affect fetal development of neuroendocrine systems, the expression of which is primarily evident in infants with high negative affectivity. Prenatal stress and infant temperamental negativity may independently or interactively increase the risk of harsh or insensitive mother-infant interactions, which may increase infant cortisol activity. Future studies may want to code and evaluate the quality of mother-infant interaction as a potential mediator of the link between prenatal distress and infant HPA activity. An intriguing line of research suggests epigenetic mechanisms that enhance or reduce gene expression may link pre- and postnatal experiences with child health and developmental outcomes (Monk, Spicer, & Champagne, 2012). Shared genes between mother and child may partially account for the relation between maternal prenatal depressive symptoms and infant temperamental negativity. The interactive influence of maternal depressive symptoms and infant temperamental negativity on infant cortisol at 12 weeks of age could reflect a gene-environment interaction, and the impact of infant negativity on later maternal depression and social support could reflect gene-environment correlations.

Limitations to the analyses should be considered. First, infant temperamental negativity was determined by maternal report. However, the IBQ is a widely used measure of temperament that was designed to minimize parental biases and has shown convergent validity with observational measures (Putnam, Helbig, Gartstein, Rothbart, & Leerkes, 2014). Similar links between mother prenatal stress and infant temperament using observer ratings of temperament have been found (Dougherty et al., 2013). We addressed this concern by statistically adjusting for mother's negative mood when she reported temperament. Second, we did not measure pregnancy cortisol and cannot evaluate *in utero* hormone exposure. Third, we did not collect genetic measures. However, because HPA activity has a heritable component, we adjusted for maternal cortisol at 12 weeks in our prediction of infant cortisol. Fourth, the mother-infant interaction task did not elicit significant cortisol reactivity; interpretation of results should be limited to the intensity of total cortisol secretion across the task. Fifth, the interpretation of the health implications of elevated infant AUCg is complicated. There is considerable diversity in the form or direction of the impact of adversity on developing HPA activity, and both exaggerated and attenuated patterns have

been linked to long-term psychological and physical health problems. It will be important for later studies to link infant cortisol output to health and developmental outcomes. Finally, only pregnant women of Mexican origin who reported very low family income were included. Although other studies have found effects of acculturation level on infant outcomes in Mexican American samples (e.g., D'Anna-Hernandez et al., 2012), the low acculturation across our sample may have limited power to detect potential influences of acculturation on infant outcomes. Caution should be taken in generalizing results to other racial/ethnic groups, higher income groups, or more acculturated Mexican Americans.

In conclusion, this study provides insight into the effects of prenatal psychosocial experiences on infant biological regulatory systems in Mexican American families at high risk of perinatal depression and child health and developmental disparities. Our results suggest that prenatal maternal depressive symptoms and low prenatal social support predicted higher cortisol activity at 3 months of age for infants with high temperamental negativity. However, temperamental negativity did not enhance the benefits of a positive prenatal environment. Mothers reporting higher temperamental negativity in their infants experienced a decline in social support and an increase in depressive symptoms from the prenatal period to 12 weeks postpartum relative to mothers with temperamentally “easier” infants. The continuation of a negative postpartum environment and increased susceptibility of the infant may pose future risks for both maternal and child adjustment.

ACKNOWLEDGMENTS

This research was funded by the National Institute of Mental Health (R01 MH083173-01). We thank the mothers and infants for their participation; Kirsten Letham, Anne Mauricio, and Monica Gutierrez for their assistance with data collection and management; Dr. Dean Coonrod and the Maricopa Integrated Health Systems for their assistance with recruitment; and the interviewers for their commitment and dedication to this project.

Contract grant sponsor: National Institute of Mental Health

Contract grant number: R01 MH083173-01

The funding source had no role in study design, collection, analysis, interpretation, or writing of the report; or in the decision to submit the article for publication.

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FIGURE 1.

Prenatal depressive symptoms and infant temperamental negativity effect on infant cortisol AUCg. For display purposes, low negativity and low depression were set at 1 SD below the sample mean; high negativity and high depression were set at 1 SD above the sample mean.

FIGURE 2.

Prenatal social support and infant temperamental negativity effect on infant cortisol AUCg. For display purposes, low negativity and low social support were set at 1 SD below the sample mean; high negativity and high social support were set at 1 SD above the sample mean.

Table 1**Sample Demographics**

Prenatal Marital Status – N (%)	
Married or Living W/Partner	249 (77%)
Not married or living W/Partner	73 (23%)
Education – N (%)	
0 Through 8 Years of School	87 (27%)
Some High School Completed	103 (32%)
High School Graduate	86 (27%)
Some College, Vocational or Technical School	26 (8%)
College Degree (BS/BA) or Above	20 (6%)
Family Income N (%)	
\$10,000	101 (33%)
\$10,001–\$15,000	87 (28%)
\$15,001–\$20,000	37 (12%)
\$20,001–\$25,000	40 (13%)
\$25,001–\$30,000	16 (5%)
\$30,001–\$40,000	17 (5%)
\$40,000	12 (4%)
Birth Weight (g) – Range; M (SD)	1190–4935; 3389 (464)
Low Birth Weight (<2500 g); N(%)	2 (1%)
Gestational Age (wks) – Range; M (SD)	26–42; 39.3 (1.4)
Preterm Birth (<37 wks); N(%)	10 (3.1%)
Prenatal Depressive Symptoms – Range; M (SD)	0–25; 6.1 (5.5)
Above Clinical Cutoff (EPDS 13)–N(%)	43 (13.4%)
Prenatal Social Support – Range; M(SD)	4–68; 50.9 (15.7)
12 wk Infant AUCg (Non-Transformed)–M (SD)	17.3 (14.6)

Table 2

Zero-Order Correlations^a

	1	2	3	4	5	6	7	8	9	10	11	12
1. Prenatal Social Support	1.0											
2. Prenatal Depressive Symptoms	-.28*	1.0										
3. Temp. Negativity	-.06	.26*	1.0									
4. Mother's Age	-.12*	.00	-.07	1.0								
5. Education (Yrs)	.10	.06	.06	-.28*	1.0							
6. Household Income	.11	-.02	.08	.06	.25*	1.0						
7. 12 Wk Depression	-.20	.39*	.28*	.08	.00	.11	1.0					
8. 12 Wk Social Supp	.65*	-.27*	-.11	-.04	.23*	.14	-.31*	1.0				
9. Breastfeeding ^a	.01	.03	.05	.15*	-.08	.06	.01	.06	1.0			
10. Time of Day ^b	-.18*	-.09	.01	.05	-.07	.09	-.03	-.11	-.04	1.0		
11. Last Feeding ^c	-.02	-.03	-.03	.23*	.06	-.07	.06	.12	-.05	-.10	1.0	
12. Mother AUC ^g	.15*	-.06	.02	-.05	.11	.01	-.01	.08	.04	-.58*	.11	1.0
13. Infant AUC ^g	.02	.04	.10	.05	.01	-.08	.24*	.02	.08	-.22*	.09	.22*

^a Pearson correlations; "Social Supp"=Social Support; "Depression"=Depressive symptoms; "Temp"=Temperamental.

^a Coded 0=bottle-feeding only; 1=partial or exclusive breast-feeding.

^b Calculated in minutes since midnight.

^c Coded 1=less than an hr ago; 2=1-2 hr ago; 3=2-3 hr ago; 4=3-4 hr ago; 5=more than 4 hr ago.

^d Log-transformed.

* $p < .05$.