Summary of the Project Aims

The overarching objective of this project was to evaluate the influence of a woman’s life adversity prior to her pregnancy on her psychological, neuroendocrine and proinflammatory profile during her pregnancy. In addition, the effect of maternal antenatal life adversity on infant outcomes was evaluated in an exploratory manner. The central hypothesis of this proposal was: adverse experiences prior to pregnancy primes stress response systems and leads to increased psychological stress, neuroendocrine activation, and dysregulate proinflammatory cytokine levels. Such alterations in maternal stress-response systems may contribute to poor infant outcomes. Women were enrolled during the second trimester of their pregnancy and the following specific aims were determined:

Specific Aims

1. Examine the relationship between maternal childhood adversity and maternal psycho-neuroendocrine-inflammatory profile during pregnancy.

2. Evaluate maternal risk and protective factors as moderators of maternal PNI profile during pregnancy.

3. Explore the relationship among maternal childhood adversity, maternal PNI profile during pregnancy, and neonatal outcomes.

Theoretical / Conceptual Model

The conceptual model posited potential linkages whereby maternal antenatal adverse experiences influence her psychological well-being, neuroendocrine activity, and
proinflammatory cytokine levels during pregnancy, ultimately affecting neonatal outcomes. For the purposes of this study, life adversity was conceptualized as a woman’s pre-pregnancy exposure to adverse experiences prior to 18 years of age, originating from childhood and family experiences and/or related to low SES. Life adversity was measured by asking pregnant women to complete the Child Trauma Questionnaire (CTQ). This instrument will provided information as to the woman’s experience of adversity during her childhood. The experience of pregnancy is a normal life event; however, it is characterized by marked psychological, social, and physiological changes and for most women this life change results in psychological stress, requiring adaptation.

The proposed model posits that women who have experienced greater adverse experiences during their childhood will respond to their pregnancy with greater stress perception (general stress), depression (risk), anxiety (state), and mood disorder. Additionally, greater childhood adversity will result in elevated neuroendocrine (cortisol) and proinflammatory (IL-6) cytokine levels during pregnancy. This model is supported by evidence derived from animal and human studies that identify early life adversity as a vulnerability factor that gives rise to an adult phenotype characterized by a heightened stress reactivity. This heightened stress reactivity is characterized by greater psychological, cortisol, and proinflammatory responses to stressful life events (Entringer et al., 2008). It is further, hypothesized that moderating factors will influence the effect of antenatal adversity (i.e. protective factor). Maternal moderating factors evaluated included levels of social support available to a woman during her pregnancy. Greater social support during pregnancy was posited to lessen (i.e. buffer) the impact of antenatal life adversity on outcomes. Lastly, the increased intensity of the woman’s stress response during pregnancy
(psychological, cortisol, and IL-6) was posited to result in worse neonatal outcomes (Entringer, et al., 2008). The neonatal outcomes evaluated included: birthweight and gestational age.

**Overview of Design**

Pregnant women were evaluated at two times across pregnancy. Pregnancy has four trimesters; 1st trimester is 1-12 weeks, 2nd trimester 13-26 weeks, and 3rd trimester 27-42 weeks gestation, and 4th trimester or postpartum is within the first 6 weeks after delivery. Recruitment identified participants early in gestation but data collection did not begin until 2nd trimester. Initial data collection, Time 1 was in second trimester (16-24 weeks gestation), while Time 2, was in third trimester (28-32 weeks gestation).

Pregnant women completed the same questionnaires at both Time 1 and Time 2. These included Perceived Stress Scale (PSS) to evaluate stress perception, Edinburgh Depression Scale (EDS) and Center for Epidemiological Studies Depression Scale (CES-D) to evaluate depressive risk, State and Trait Anxiety Scale (STAI-state) to evaluate anxiety, Profile of Mood State (POMS-65) to evaluate mood, and Social Provisions Assessment (SPA) to evaluate Social Support. Additionally, women completed a demographic and health questionnaire. Pregnant women completed self-report instruments to evaluate prior life adversity; which includes, Childhood Trauma Questionnaire (CTQ) after delivery.

Neuroendocrine activation during pregnancy was evaluated by measuring cortisol in hair samples. Hair cortisol provides a cumulative index of stress over the past 3 months. Hair cortisol was measured at both second and third trimester (T1 and T2 respectively). Proinflammatory immune activation was determined by measuring circulating IL-6 in blood samples during both the second (T1) and third trimesters (T2) of pregnancy. Neonatal outcomes
were assessed to provide exploratory data to evaluate the association between prenatal stress and neonatal development. Birth data (birthweight and gestational age) were obtained from medical records.

**Enrollment and Data Collection**

This study was approved by the sponsoring agency Institutional Review Board. Data were collected from November 2012 to November 2014. Ninety-five pregnant healthy low-risk pregnant women were enrolled during their first or second trimester of pregnancy from a large academic medical center. Of the ninety-five women enrolled, fourteen women withdrew from the study; and only a portion completed all measures for each time point. For Time 1, sixty-four women provided data for all biologic variables and all questionnaires; for Time 2, forty-four women provided data for these measures. For hair cortisol assessment, (N=66, N=52 at T1 and T2 respectively) many but not all, agreed to do hair sampling for cortisol analysis.

**Summary of Results**

Key findings from this prospective study demonstrate at both mid-pregnancy and late pregnancy, maternal childhood adversity was associated with greater perceived stress, depressive (risk), anxiety, and mood disorder, in addition to lower social support at mid-pregnancy and late-pregnancy. Additionally, maternal childhood adversity was correlated with pro-inflammatory cytokine IL6 at late-pregnancy.

In this sample, social support moderated the association between childhood adversity and birthweight. These results indicate women experience greater maternal childhood adversity in combination with lower social support during their pregnancy, delivered infants with lower birthweight; while women with greater maternal childhood adversity with greater social
support had greater birthweight infants. This suggests social support buffers the negative impact of maternal childhood adversity on infant birthweight. Similarly, social support also moderated the association between childhood adversity and gestational age, such that social support buffered the negative effect of maternal childhood adversity on lower gestational age. As such, these results suggest that harmful effects of maternal childhood adversity on birthweight and gestational age appear to be worse in women with low social support in late-pregnancy. This study is consistent with these findings, showing women with greater social support had a buffering effect on adverse neonatal outcomes (i.e., birthweight and gestational age) (Collins, Dunkelschetter, Lobel, & Scrimshaw, 1993).

Maternal childhood adversity moderated the association between proinflammatory cytokine IL-6 on birthweight when controlling for BMI, feelings about pregnancy, pregnancy complications. Further, women with a history of greater childhood adversity exhibited higher circulating levels of IL-6 late-pregnancy, which influenced neonatal outcomes by delivering earlier in gestation and lower birthweight infants. These findings are consistent with earlier research demonstrating that disruption in the balance of pro- and anti-inflammatory cytokines is implicated in adverse pregnancy outcomes, such as premature delivery, and intrauterine growth restriction (Challis et al., 2009).

In an exploratory analysis hair cortisol during pregnancy was evaluated with respect to perceived stress during pregnancy. Hair cortisol is a non-invasive way to index chronic stress. For the purposes of this study, hair cortisol was measured at two time points (second and third trimester) as an approximate measure of HPA activity over a 3-month time interval. The findings revealed that higher levels of hair cortisol at T2 were positively correlated with perceived stress.
measured at T1 but not at T2. The lag in time interval between these two related variables is consistent with the concept that hair cortisol reflects stress levels from the previous three months. As such, hair cortisol may not be expected to reflect the most recent assessment of perceived stress, but rather the levels of stress measured earlier in time. In addition, findings from this dissertation research revealed that women who expressed less positive feelings about their pregnancy had higher levels of hair cortisol at mid-pregnancy (T2).

Recommendations

This research adds to the body of evidence exploring maternal risk and protective factors moderating the impact of childhood adversity on maternal health and neonatal outcomes. The findings can contribute to improved approaches to identify and stratify risk for adverse maternal-infant health outcomes, as well as guide the development of early intervention programs and health policy for women who are pregnant or who plan to become pregnant. Further, the findings can stimulate new approaches to improve mother-infant health by informing policy regarding universal screening of women for early life adversity, which impacts maternal stress perception and depressive risk during pregnancy. Improving mother-infant health today can markedly reduce overall cost of health across the lifespan.

How the Grant Assisted Me to Complete My Research

Receiving the Doris Bloch Research Grant allowed me to explore a new non-invasive way to measure cortisol during pregnancy. Additionally, the grant provided me the necessary funds to offset payment to participants, to understanding stress during pregnancy and maternal-infant
health outcomes. Without these necessary funds, I would not have been able to explore important questions that may help understand the unique bio-behavioral characteristics women experience during pregnancy.

References


