RESEARCH ARTICLES

Prenatal Maternal Anxiety and Depression Predict Negative Behavioral Reactivity in Infancy

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The effects of maternal antenatal and postnatal anxiety and depression on infant negative behavioral reactivity were examined in a sample of 22 mother–infant pairs. Ma-

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ternal anxiety and depression were assessed by standardized measures during the third trimester of pregnancy and postpartum. Infant negative behavioral responses to novelty were assessed using a previously validated measure at 4 months of age. Maternal anxiety and depression during the prenatal, but not the postnatal period, were related to infant negative behavioral reactivity to novelty. These data illustrate that prenatal maternal psychological state can exert persisting influences on human infant behavior.

There is strong evidence across a wide range of species that early postnatal experiences influence the development of individual differences (Coplan et al., 1996; Dawson & Ashman, 2000; Levine, 1957). Maternal stress, anxiety, and depression during infancy have pervasive influences on development including enhanced stress reactivity, poor emotional regulation, and impaired cognitive development (Coghill, Caplan, Alexandra, Robson, & Kumar, 1986; Dawson, Ashman, & Carver, 2000; Downey & Coyne, 1990; Essex, Klein, Cho, & Kalin, 2002; Hammen, Burge, Burney, & Adrian, 1990; Kaplan, Bachorowski, Smoski, & Hudenko, 2002). These effects appear to be mediated by disturbances in the quality of mother–child interactions (Cohn, Campbell, Matias, & Hopkins, 1990).

The influence of maternal experiences during pregnancy on later infant development has largely been neglected in human research. This is surprising because extensive animal research has documented lifelong effects of exposure to stress during prenatal development (Chapillon, Patin, Roy, Vincent, & Caston, 2002; Schneider, 1992; Weinstock, 2001). Recent studies have reported that maternal anxiety and depression during pregnancy shape fetal behavioral patterns (DiPietro, Hilton, Hawkins, Costigan, & Pressman, 2002; Monk, Myers, Sloan, Ellman, & Fifer, 2003) and predict higher cortisol and norepinephrine and lower Brazelton scores in the newborn (Jones et al., 1998; Lundy et al., 1999). These findings suggest that human maternal psychological state during pregnancy influences the development of the fetus, presumably through alterations in maternal physiology. Consideration of the contribution of maternal psychological state during pregnancy to subsequent infant behavior may improve the ability to identify significant factors that contribute to the development of individual differences in behavior seen in infancy and childhood.

The few studies examining the impact of prenatal experiences on development in humans are limited either by the use of retrospective designs or parent reports of child behavior. These studies have found that maternal stress, anxiety, and depression during pregnancy is related to emotional disturbances and difficult temperament in the offspring (Luoma et al., 2001; Meijer, 1985; O'Connor, Heron, & Glover, 2002; O'Connor, Heron, Golding, Beveridge, & Glover, 2002; Papousek & von Hofacker, 1998; Stott, 1973; Van den Bergh, 1990; Ward, 1991). However, retrospective report of pregnancy is problematic because of a number of factors, including child's current temperament, which might bias recall of experiences dur-

ing pregnancy. Subjective description of child behavior by the parent is confounded by the parent's psychological state at the time of reporting. Only one study was identified that demonstrated an association between maternal anxiety during pregnancy and child behavior using both a prospective method and objective behavioral observations of the child (Huizink, de Medina, Mulder, Visser, & Buitelaar, 2002). This study found that the infants of mothers who reported higher levels of anxiety during pregnancy displayed poorer attention regulation at 3 and 8 months. Clearly there is a need for further prospective human studies that employ objective assessments of child behavior to differentiate the effects of prenatal and postnatal maternal anxiety and depression on development.

The goal of this study was to examine the contribution of maternal psychological state in a healthy group of women during the prenatal and the early postnatal period on several direct indicators of infant temperament. It has been established that stable individual differences exist in infants' behavioral responses to challenges such as novelty (Schwartz, Snidman, & Kagan, 1999). These individual differences seen in infancy predict fearful and anxious behavior later in childhood (Kagan, Snidman, & Arcus, 1998). Research with both rodents and nonhuman primates has demonstrated that an important consequence of prenatal exposure to stress is greater reactivity to novelty challenges (Clarke, Wittwer, Abbott, & Schneider, 1994; Schneider, 1992; Vallee, Mayo, Dellu, Moal, & Maccari, 1997). If maternal mood during pregnancy affects later infant negative behavioral reactivity, than infants of mothers who were anxious or depressed during pregnancy should display greater negative behavioral reactivity to novelty even after accounting for postnatal maternal mood. To examine the discrete influence of these factors in the prenatal period, maternal levels of anxiety and depression were assessed with standardized self-report measures during the third trimester of pregnancy and after birth (Radloff, 1977; Spielberger, 1983). In addition, infants' negative behavioral reactivity to challenge was examined using a standardized laboratory procedure designed to assess behavioral responses to novel stimuli (Kagan et al., 1998).

METHODS

Participants

Participants in this study were 22 mother–infant pairs recruited serially from an obstetric clinic at the University of California, Irvine. Women gave informed consent for all aspects of the protocol, which was approved by the institutional review board for protection of human participants. Women in this sample had healthy singleton pregnancies, were not diagnosed with a psychological disorder, and refrained from smoking or alcohol use during pregnancy according to participant report and review of medical records. At the time of the first assessment, the 22

mothers ranged in age from 18 to 36 years old ($M = 28$ years, $SD = 5.4$ years), 17 of the women were married, and 12 were primiparous. Annual household income for this sample ranged from \$10,000 to \$90,000. Fifteen of the women were non-Hispanic White and 6 were Hispanic White. This sample is representative of low-risk pregnancies seen at this clinic. The infants of these women (12 girls and 10 boys) were assessed at 4 months of age. All infants were born at term (M gestational age = 39.3 weeks, $SD = 2.1$ weeks) and were the appropriate weight for their gestational age ($M = 3627.5$ g, $SD = 715.1$ g). Fourteen infants were delivered vaginally, and eight were delivered by cesarean section.

Procedures

In this longitudinal study, women reported on their psychological state two times, once during the third trimester of pregnancy and once after delivery. In addition, prenatal medical history was obtained. Infants' response to novelty was assessed utilizing a standardized observational assessment of negative behavioral reactivity at 4 months of age (Kagan & Snidman, 1991; Kagan et al., 1998).

Measures

Obstetric history.   Prenatal medical history and birth outcome were gathered through review of the mothers' and the infants' medical records, and a score assessing medical risk for adverse birth outcome was derived (Hobel, 1982). Factors considered included pregnancy-induced hypertension, gestational diabetes, and previous pregnancy resulting in preterm delivery, spontaneous abortion, stillbirth, or ectopic pregnancy. In addition, parity, mode of delivery, gestational age at birth, and birth weight were recorded.

Maternal psychological assessments.   Maternal anxiety and depression were assessed during pregnancy at 32 weeks gestation and at 8 weeks after delivery. State anxiety was measured using the state anxiety subscale of the State–Trait Anxiety Inventory (STAI; Spielberger, 1983). This 10-item scale assesses the extent to which participants are experiencing anxiety-related symptoms or emotions using a 4-point Likert scale ranging from 1 (*not at all*) to 4 (*very much*). State anxiety scores can range from a minimum of 10 to a maximum of 40. The STAI has been used for research purposes with pregnant and nonpregnant samples (Rini, Dunkel-Schetter, Wadhwa, & Sandman, 1999). The STAI has good internal consistency, with an alpha of .77 in this sample. Depression was evaluated using the Center for Epidemiological Studies Depression Inventory (CES-D; Radloff, 1977). Responses to each of the 10 items of this measure were recorded on a 4-point Likert scale with a range of 0 to 3. Anchor points, in terms of days per week, were "rarely or none of the time (less than 1 day)" to "most or all of the time

(5–7 days)." The final score can span from 0 to 30, with a higher score indicating greater impairment. A score of 22 or higher suggests a possibility of major depression, and a score of 15 to 21 indicates that the participant may be suffering from mild to moderate depression (Radloff, 1977). The CES-D has good internal consistency, with an alpha of .94 for this sample. The CES-D is a commonly used instrument for the study of depression in the general population and has been validated in pregnant samples (Marcus, Flynn, Blow, & Barry, 2003). Scores on the CES-D during pregnancy are associated with birth outcome and other negative health consequences (Lundy et al., 1999; Marcus et al., 2003).

Infant behavioral reactivity.   Infant behavioral reactivity was assessed at 4 months using the Harvard Infant Behavioral Reactivity Protocol, a standard battery designed by Kagan, Snidman, and colleagues to assess behavioral reactivity to novelty in infants, an early correlate of shy or inhibited temperament (Kagan & Snidman, 1991). Infants were assessed at 4 months of age because 4 months is the youngest age typically examined using this paradigm and because behavioral responses at 4 months are predictive of later behavior. Each assessment began with the infant rested, content, and reclining in an infant car seat, and consisted of 45 trials. In the first trial the mother looked and smiled at the infant for 1 min and then moved out of the infant's sight. Subsequently, the infant was presented with a series of novel sensory stimuli. First, a speaker was placed 10 in. (25.4 cm) in front of the infant, and an audiotape of several voices speaking eight different sentences that were each 6 sec in length was played (e.g., "Hello baby, how are you today"). Five seconds of silence separated each utterance. This was followed by the presentation of a series of eight tastes presented with an eyedropper. Taste 1 was water, Tastes 2 to 4 were a solution of sugar and water, Tastes 5 to 7 were lemon juice diluted with water, and Taste 8 was water. The examiner then moved a sequence of colorful mobiles back and forth in front of the infant. The first mobile had one toy, the second had three, and the third had seven. Each mobile was presented for 20 sec. The series of three mobiles was presented three times. In the next five trials, a cotton swab was held to the infant's nostrils for 5 sec. The swab was dipped in water once, in diluted alcohol four times, and then in water again. The infant then heard a tape recording through a speaker of a female voice speaking three different syllables (*ma, pa, ga*) three times each at three volumes (70, 80, 90 dB) for a total of nine trials. The experimenter then popped a balloon behind the infant's head. Finally, the mother stood smiling in front of the infant for 1 min without touching or speaking to her child.

Videotapes of infants were coded for frequency of motor activity and fretting or crying by the Harvard Infant Behavioral Reactivity study team (Kagan & Snidman, 1991). In response to this paradigm, infants who are high in both motor activity and crying are characterized as being high in negative behavioral reactivity and are at risk for the development of shyness or behavioral inhibition later in child-

hood (Kagan et al., 1998). Coders were blind to study hypotheses and any other information about mother–infant pairs. Tapes were coded separately for two types of behaviors. Motor activity was defined as the number of times during the 45 trials that the infant did any of the following: move both arms from above the elbow at least 30°, move both legs at least 30°, or arch the back so that the chest comes forward and the back is off the chair. The crying score was determined by recording the number of trials (out of a total of 45 trials) in which crying, fretting, or fussing occurred. Interrater reliability was calculated on one third of the tapes and was .84 for motor activity and .83 for number of trials in which crying occurred.

RESULTS

Maternal Psychological Assessments

The distribution of scores on the STAI and CES-D and the association between these measures at the pregnancy and the postpartum assessment are displayed in Tables 1 and 2. Distributions for the STAI were similar to the distribution found by Spielberger (1979), who reported state anxiety scores for women between 23 and 32 years old as 18.6 ($SD = 6.8$) and for 33 years old and older as 18.2 ($SD = 5.8$). Scores on the CES-D were assessed with respect to standardized cutoffs using this measure. During pregnancy 15% of the sample scored between 15 and 21, and 27% scored 22 or higher. At the postpartum assessment 5% of the sample scored between 15 and 21, and 20% scored 22 or higher. There were no significant differences between pregnancy and postpartum assessments of anxiety, $t(22) = 0.46$, *ns,* and depression, $t(22) = 1.1$, *ns.* In addition, prenatal and postnatal anxiety, $r(22) = .55, p = .01$, and prenatal and postnatal depression, $r(22) = .55, p = .01$, were significantly correlated. Thirty percent of the variance in anxiety and depression was shared between prenatal and postpartum measures, suggesting that there was a change in the women's psychological state between the prenatal and postpartum period. Concurrent measures of anxiety and depression were highly correlated

TABLE 1
Mean Levels of Anxiety and Depression During the Third Trimester
of Pregnancy and Postpartum

	Prenatal			Postpartum		
	M	*SD*	*Range*	*M*	*SD*	*Range*
STAI	20.5	6.1	10–30	19.9	16.7	10–38
CES-D	14.9	10.2	2–34	12.6	11.1	0–48

Note.   STAI = State–Trait Anxiety Inventory; CES-D = Center for Epidemiological Studies Depression Inventory.

TABLE 2
Pearson Product–Moment Correlation With Prenatal and Postnatal Anxiety
and Depression and Infant Behavior

	1. STAI Prenatal	2. CES-D Prenatal	3. STAI Postpartum	4. CES-D Postpartum	5. Infant Behavior
1. STAI Prenatal	—				
2. CES-D Prenatal	.74**	—			
3. STAI Postpartum	.55**	.65**	—		
4. CES-D Postpartum	.40*	.55**	.87**	—	
5. Infant Behavior	.44*	.52*	.12	.14*	—

Note. STAI = State–Trait Anxiety Inventory; CES-D = Center for Epidemiological Studies Depression Inventory.
*$p < .05$. **$p < .01$.

during pregnancy, $r(22) = .74$, $p = .0001$, and postpartum, $r(22) = .87$, $p = .0001$. Neither the presence of medical risk factors nor mode of delivery was related to pre- or postnatal maternal anxiety or depression (all $ps > .14$).

Infant Negative Behavioral Reactivity

In response to presentation of novel stimuli, infants displayed an average of 141 ($SD = 49.6$, range = 58–246) incidences of motor activity. Crying occurred in an average of 10.4 ($SD = 11.4$, range = 0–41) of the 45 trials. The crying score was positively skewed. A square root transformation brought the skew into an acceptable range. A negative behavioral reactivity score was created by standardizing and summing the motor activity score and the transformed crying score. Thus, a high behavioral reactivity score reflected high levels of both motor activity and crying. Mean comparisons indicated that infant negative behavioral reactivity to novelty was not significantly affected by sex of the infant, $t(22) = 1.7$, *ns;* the presence of medical risk factors, $t(22) = 0.3$, *ns;* or the mode of delivery, $t(22) = 0.1$, *ns.*

Maternal Psychological State and Infant Behavioral Reactivity

To examine the influence of maternal psychological state during pregnancy and postpartum on infant's negative behavioral responses to novelty, four simple regressions were performed. It was found that prenatal maternal anxiety accounted for 20% of the variance in infant negative behavioral reactivity ($\beta = .44$, $t = 2.2$, $p = .04$). These data are depicted in Figure 1. Similarly, prenatal depression accounted for 27% of the variance in infant negative behavioral reactivity ($\beta = .52$, $t = 2.7$, $p = .01$). These data are depicted in Figure 2. Neither postnatal anxiety ($R^2 = .01$, $\beta =$
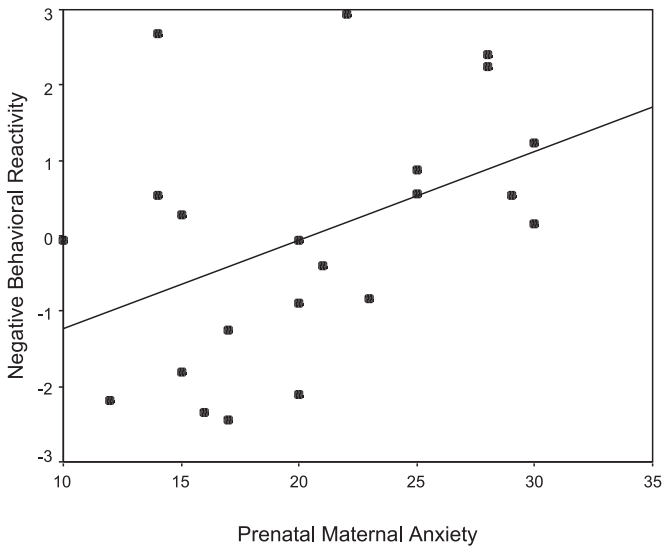
FIGURE 1   Maternal anxiety during the third trimester of pregnancy and infant negative behavioral reactivity to novelty.
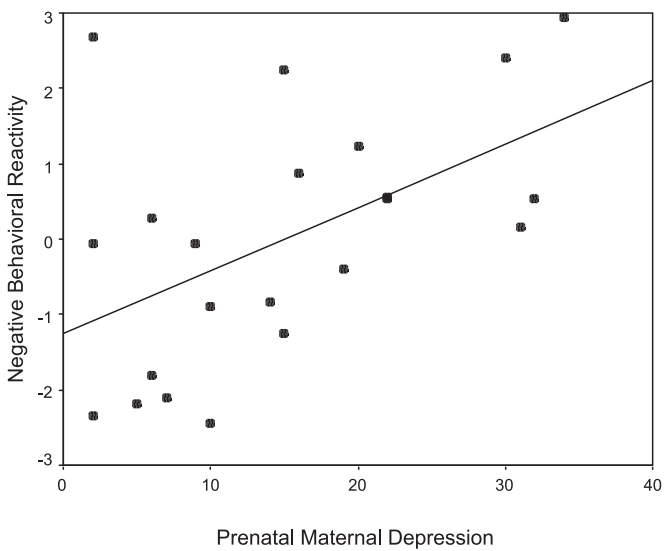

FIGURE 2   Maternal depression during the third trimester of pregnancy and infant negative behavioral reactivity to novelty.

.11, $t = 0.48$, *ns*) nor depression ($R^2 = .01$, $\beta = .12$, $t = 0.52$, *ns*) accounted for a significant portion of the variance in infant negative behavioral reactivity. See Table 2 for a summary of the correlations between maternal and infant measures. To examine whether prenatal maternal psychological state accounted uniquely for any variance in 4-month-old infants' negative behavioral reactivity, above and beyond that accounted for by postnatal psychological state, two hierarchical regressions were performed for anxiety and depression entering postnatal psychological state first. Prenatal anxiety ($\Delta R^2 = .21$, $p = .04$) and depression ($\Delta R^2 = .30$, $p = .01$) accounted for a significant portion of the variance after controlling for postnatal psychological state. The ΔR^2 is larger than the R^2 for the simple regressions. This is due to the suppression effect that occurs when both prenatal maternal psychological state and postnatal maternal psychological state are added to the regression models predicting infant behavior. The regression models showing this effect are displayed in Tables 3 and 4 (for a discussion of suppression, see Netter, Kutner, Nachtsheim, & Wasserman, 1996).

TABLE 3
Regression Model Examining Whether Prenatal Maternal Anxiety
Accounted Uniquely for Any Variance in Infants' Negative Behavioral
Reactivity Above and Beyond Postnatal Maternal Anxiety

	R^2	ΔR^2	β	*Partial Correlation*
Model 1	.01			
Postpartum STAI			.11	.11
Model 2	.22*	.21*		
Postpartum STAI			−.19	−.16
Prenatal STAI			.55*	.45*

Note.   STAI = State–Trait Anxiety Inventory.
*$p < .05$.

TABLE 4
Regression Model Examining Whether Prenatal Maternal Depression
Accounted Uniquely for Any Variance in Infants' Negative Behavioral
Reactivity Above and Beyond Postnatal Maternal Depression

	R^2	ΔR^2	β	*Partial Correlation*
Model 1	.01			
Postpartum CES-D			.12	.12
Model 2	.31**	.30**		
Postpartum CES-D			−.24	−.24
Prenatal CES-D			.66*	.55*

Note.   CES-D = Center for Epidemiological Studies Depression Inventory.
*$p < .05$. **$p < .01$.

DISCUSSION

Maternal anxiety and depression during the third trimester of pregnancy, but not postpartum, were associated with individual differences in infants' behavioral regulation at 4 months. The offspring of mothers who were higher in anxiety and depression during pregnancy displayed greater negative behavioral reactivity to novelty. Notably, this association remained after controlling for postpartum maternal psychological state, indicating that prenatal experiences could be responsible for this association. The selective effects of prenatal experiences on behavioral reactivity support the hypothesis that the prenatal environment exerts programming effects on the fetus with consequences for infant behavior (Barker, 2002; Welberg & Seckl, 2001).

Negative behavioral reactivity in response to novelty in infancy may have implications for subsequent behavioral problems. Infants who are easily aroused by varied stimulation are more likely to become behaviorally inhibited as young children (Kagan et al., 1998). Difficulty adapting to the presentation of novel sensory stimuli in infancy is predictive of later behavioral problems such as adolescent social anxiety (Schwartz et al., 1999). The association reported here between anxiety and depression during pregnancy and behavioral reactivity to novelty in infancy suggests that a fetus developing in the environment of a more anxious and depressed mother has an increased risk for behavioral inhibition and perhaps later anxiety disorders. The relation between maternal psychological state during pregnancy and infant behavior is particularly significant because women in this sample did not suffer from clinical levels of anxiety or depression, conditions that may exert stronger effects. However, because of the relatively small sample size, caution is necessary in interpretation of these data. Further investigation of these findings with a larger sample size is necessary.

The differential impact of prenatal and postnatal maternal psychological state on the fetus and infant may by due to the variation in mechanisms during these two periods. Maternal psychological state during the postnatal period influences the infant through alterations in mother–child interactions (Cohn et al., 1990). During pregnancy, maternal psychological state is associated with hormonal changes, including changes in the stress hormones of the hypothalamic-pituitary-adrenocortical (HPA) and placental axis (Sandman, Wadhwa, Chicz-DeMet, Dunkel-Schetter, & Porto, 1997). Evidence suggests that elevations in these stress hormones are associated with impaired central nervous system (CNS) functioning in the fetus (Sandman, Wadhwa, Chicz-DeMet, Garite, & Porto, 1999) and disregulation of stress responses in the newborn (Davis et al., 2004). Prenatal anxiety and depression could affect maternal and fetal stress hormone production, thus influencing fetal CNS structure and function (Sandman et al., 1999). The impact of maternal mood during pregnancy on infant behavior shown here may be mediated by such hormonal changes.

These findings demonstrate an association between maternal anxiety and depression during pregnancy and infant behavior and add to the small number of previous studies with humans indicating that maternal mood during pregnancy has persisting effects on the functioning of the offspring. To understand the processes by which maternal psychological state affects infant development, it is necessary to assess maternal emotional state during both the prenatal and the postnatal period. Studies or interventions focused only on postnatal maternal psychological state may miss critical factors that contribute to the development of her offspring.

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