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Maternal Psychological Distress During Pregnancy in Relation to Child Development at Age Two

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Concern exists that a constellation of negative maternal emotions during pregnancy generates persistent negative consequences for child development. Maternal reports of anxiety, pregnancy-specific and nonspecific stress, and depressive symptoms were collected during mid-pregnancy and at 6 weeks and 24 months after birth in a sample of healthy women with low risk pregnancies. Developmental assessment and cardiac vagal tone monitoring were administered to 94 children at age 2. Higher levels of prenatal anxiety, nonspecific stress, and depressive symptoms were associated with more advanced motor development in children after postnatal control for each psychological measure; anxiety and depression were also significantly and positively associated with mental development. Mild to moderate levels of psychological distress may enhance fetal maturation in healthy populations.

The daughter of Virata . . . {was} exceedingly afflicted by grief on account of the death of her husband . . . They all feared that the embryo in her womb might be destroyed. The Mahabharata, Book 14, Section LXII (~ 500 BC)

He's not right. It was grief that caused the boy to be like he is. Wavey was carrying him when Sevenseas Hector went over. Lost her husband. The Shipping News. 1993, A. Proulx, *p* 132

Sentiments that the emotional life of the pregnant woman influences the development of her fetus are ubiquitous and persistent throughout culture and history. More recently, an aggregating body of scientific evidence and ensuing media coverage has moved the notion that the fetus and pregnancy are put in jeopardy by a constellation of maternal indicators of psychological distress, including stress, anxiety, and depression more prominently into academic and public awareness. Most research has been directed at detecting proximal effects, and a substantial body of evidence has accrued indicating that higher levels of distress during pregnancy are associated with shortened gestation and/or restricted growth, although results are by no means uniform (for reviews see Kofman, 2002; Paarlberg, Vingerhoets, Passchier, Dekker, & van Geijn, 1995).

There have been only a handful of studies in which the effects of adversities experienced by a community on pregnancy outcomes have been examined. Exposure to a California earthquake was associated with a modest shortening of gestation, ranging from several days to slightly over a week in a sample of 29 women, although these were not preterm deliveries (Glynn, Wadhwa, Dunkel-Schetter, Chicz-Demet, & Sandman, 2001). A report on the September 11th disaster, based on a sample of pregnant women who either lived in close proximity or escaped from one of the towers, found no shortening of gestation or changes in birth weight as compared to a matched control group. An increase in intrauterine growth restriction was reported, but this consequence was seen in only a small number of women in either group (Berkowitz et al., 2003). A more recent report on a subsample of this group who were interviewed before delivery found *increased* gestational duration but no effect on birth weight for women with posttraumatic stress symptoms as

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compared to those without; symptomatology covaried with both anxiety and depression (Engel, Berkowitz, Wolff, & Yehuda, 2005).

In contrast to pregnancy outcome studies, which have typically been based on large-scale epidemiologic studies of human pregnancies, animal models involving rodents have been the primary source of data on developmental effects on learning and behavior in offspring. These studies manipulate exposure of pregnant laboratory rodents to stressful events (e.g., physical restraint) and examine associations with postnatal behavior. Persistent deficits in motor development, learning behavior, and the ability to cope effectively in stressful situations have been demonstrated (Weinstock, 2001). Alterations to the hypothalamic–pituitary–adrenal (HPA) axis during prenatal development have been implicated and changes in brain structure and function of prenatally stressed rats have been documented (Fameli, Kitraki, & Sylianopolou, 1994; Henry, Kabbaj, Simon, Moal, & Maccari, 1994; Welberg & Seckl, 2001). Supportive data have been generated by several cohorts of nonhuman primates (Schneider, Moore, Kraemer, Roberts, & DeJesus, 2002). Exposure of pregnant rhesus monkeys to repeated periods of loud noise has been associated with less optimal neuromotor behavior and poorer attention during early infancy in offspring (Schneider, Roughton, Koehler, & Lubach, 1999). Few effects on early temperament were noted, with the exception of less fearfulness and distress to limitations in stressed offspring. A constellation of negative behaviors, including enhanced responsiveness to stress and dysfunctional social behavior with peers, persisted into adolescence, although nonsocial behaviors were unaffected (Clarke & Schneider, 1993; Schneider & Moore, 2000).

Studies investigating the role of prenatal psychological distress on child outcomes in humans necessarily are of strikingly dissimilar design. The vast majority of human research in this area incorporates measurement of one or more constructs of distress, most commonly anxiety, perceived stress, and depression. Psychological stress and anxiety during pregnancy are not randomly distributed phenomena but rather co-occur with other psychological and circumstantial aspects of women's lives. Thus, unlike in animal studies, in which the independent variable is administered under conditions controlled for frequency, intensity, and timing during gestation, human studies rely on selection of psychological constructs of interest and use maternal report measures to rank women within predominantly normal ranges. Although anxiety, stress, and depression may indeed reflect women's emotional responses to acute or transient circumstances during pregnancy, they are equally likely to reflect more persistent maternal psychological attributes that may be minimally related to external events. These attributes also have implications for caregiving styles after birth. Because of the profound influence of maternal psychological factors on childrearing and maternal–child interaction, strong control for postnatal expression along the same dimensions is critical to interpretation.

There have been a number of relatively recent studies that provide prospective data collection linking maternal psychological factors to subsequent child behavior and have the ability to control for postnatal exposure to maternal distress. Those that do focus on one of two types of outcomes: temperament or behavioral disorders and developmental status. The largest study focused on the former issue is a population-based study in southern England, which has generated reports that maternal prenatal anxiety, but not depression, is positively associated with greater incidence of child behavioral and emotional problems at age 4 (O'Connor, Heron, Glover, & Team, 2002; O'Connor, Heron, Golding, Beveridge, & Glover, 2002). Although these analyses contained careful control for postnatal anxiety and depression, the reliance on maternal report of behavioral problems is a limitation. It has been well established that maternal psychological attributes color the perception of child temperament and behavior (Atella, DiPietro, Smith, & St. James-Roberts, 2003; Clarke-Stewart, Fitzpatrick, Allhusen, & Goldberg, 2000; Mednick, Hocevar, & Baker, 1996; Pauli-Pott, Ries-Hahn, Kupfer, & Beckmann, 1999). Because the direction of the known associations (i.e., women reporting greater stress, anxiety, or depression also perceive their infants to be more problematic) is consistent with the findings reported in this cohort, the conclusion that biological processes underlying prenatal distress negatively influence child temperament characteristics cannot be established with certainty.

Five reports detail effects of prenatal distress beyond the neonatal period and include objective, observational measures of temperament or behavioral outcomes, and also control for postnatal maternal psychological influence. After adjusting for postnatal stress and depression, a significant, negative relation between maternal pregnancy anxiety and attentional regulation was demonstrated in a Dutch sample of infants at 3 and 8 months (Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2002), although the associated variance was less than 5%. Anxiety not specific to pregnancy was not measured. Two measures of stress were included: a daily hassles scale that was not significantly predictive and a perceived stress scale that was predictive to 8 months only. A follow-up on this sample at 27 months also found a negative association between pregnancy anxiety and attentional regulation, but none for either stress measure (Gutteling et al., 2005). Two recent reports based on a Belgian cohort find a positive association between prenatal maternal anxiety and both attention deficit disorder symptoms and externalizing problems in 8–9-year-olds ($n = 72$; Van den Bergh & Marcoen, 2004) and greater impulsivity during attentional tasks at age 15 ($n = 57$; Van den Bergh, Mennes et al., 2005). The former report included a multidimensional array of data sources (maternal, observer, and teacher reports) for the recorded behaviors, but the use of composite scores derived by principal components analysis obscures the degree to which the results were based on nonmaternal assessments. A report of a small ($n = 22$) U.S.-based sample reported significant associations between negative behavioral reactivity to novelty 4 months after birth and both prenatal anxiety and depression assessed at 32 weeks gestation, after controlling for postnatal levels (Davis et al., 2004).

Four reports focus on developmental outcomes in the first few years of life; all used Bayley Scales of Infant Development mental (Mental Development Index [MDI]) and motor (Psychomotor Development Index [PDI]) assessments. Results are inconsistent. The initial report of the Belgian cohort noted above found no associations between prenatal anxiety and MDI or PDI scores when infants were 7 months (Van den Bergh, 1990). In contrast, findings from the Dutch cohort include lower MDI and PDI scores at 8 months predicted by higher daily maternal stress at 15–17 weeks gestation but not later, and greater pregnancy anxiety at 27–28 weeks but not earlier (Buitelaar, Huizink, Mulder, Robles de Medina, & Visser, 2003). No association between prenatal anxiety and either MDI/PDI scores at age 1 was reported in another Dutch cohort, but a significant negative association between prenatal anxiety and MDI (but not PDI) scores was detected at age 2 (Brouwers, van Baar, & Pop, 2001). The only study to examine developmental outcome following a natural, community-based stressor (i.e., a severe ice storm in Quebec province) found that in a sample of 52 children of women who were pregnant during the storm, children of women who reported greater disruption to their lives, measured by maternal report of injury/danger, duration of effects, loss of property/income, and transient changes to lifestyle, had significantly lower Bayley MDI scores as well as lower MacArthur language scores at age 2 as compared to women who reported less disruption. Perceptions of the psychological stressfulness of the event, as opposed to the degree of disruption they experienced, were unrelated to outcomes (Laplante et al., 2004).

Potential effects on other aspects of development, in particular those related to autonomic dysregulation, have not been well documented. Measures of autonomic control of the heart, as indicated by either lower levels of general variability in heart rate or vagal tone, a specific measure of parasympathetic control estimated by the magnitude of the respiratory sinus arrhythmia (Berntson, Cacioppo, & Quigley, 1993; Porges, 1983), have been linked to expression of dysregulated behavior in children (Calkins & Dedmon, 2000; Huffman et al., 1998) and are sensitive to stress exposure during the early postnatal period (Porges, 1992). We have identified only one report to date of potential links between an aspect of maternal distress during pregnancy and features of child autonomic functioning. That report detected a negative association between cardiac vagal tone at 3 weeks and negative emotionality during the first, but not the third, trimester (Ponirakis, Susman, & Stifter, 1998). However, because the study sample was small and included only low-income, adolescent mothers, it is possible that these results do not generalize to the broader population of pregnant women. Nonetheless, the detection of a significant alteration in vagal tone linked to prenatal exposure suggests that the putative autonomic substrate that governs the development of behavioral expression of regulatory processes may be impacted.

The goal of the current study was to expand the limited knowledge base regarding the potential association between aspects of prenatal maternal psychological distress and both child temperament and developmental status using objective measures of each and instituting appropriate controls for postnatal psychological distress. Mid-pregnancy assessments of psychological functioning included scales that measure the most common features of distress currently examined in the literature: anxiety, stress, and depression. Accurate measurement of psychological constructs presents unique challenges during pregnancy (Lobel, 1994). A wide range of concerns unique to pregnant women has been identified as pregnancy-specific anxieties, stressors, or both (Arizmendi & Affonso, 1987; DaCosta, Brender, & Larouche, 1998; Huizink, Mulder, Robles de Medina, Visser, & Buitelaar, 2004; Kumar, Robson, & Smith, 1984; Yali & Lobel, 1999). Because pregnancy itself presents unique psychological challenges (Carlson & LaBarba, 1979; Holmes & Rahe, 1967; Zajicek & Wolkind, 1978), failure to measure pregnancy-specific sources can underestimate maternal distress. Thus we included a scale that measures both pregnancy-specific stress and contentment, thereby providing one of the only sources of data on the link between positive aspects of psychological functioning during pregnancy and development. On the basis of the existing literature, it was expected that higher indicators of distress during pregnancy would interfere with mental development, motor development, and neural control of the heart, and be positively associated with indicators of temperamental dysregulation evaluated when offspring were 2 years old. Because heightened male vulnerability to developmental risk factors is a well-known finding in general and has been implicated as a moderating factor for prenatal stress (Van den Bergh, Mulder, Mennes, & Glover, 2005), we expected effects to be more pronounced in boys.

Methods

Participants

Participants were followed longitudinally from mid-pregnancy through the child's second birthday as part of a larger study on fetal neurobehavioral development. Recruitment was restricted to low-risk, nonsmoking women at least 20 years old with singleton pregnancies and consistent pregnancy dating validated by early first trimester pregnancy testing, examination, and/or ultrasound. Forty-eight of the original 185 participants were either prospectively or retrospectively excluded based on the following: preterm labor, mild preterm delivery, or both (21; 11%); gestational diabetes (5; 3%); congenital malformation (2; 1%); fetal death in utero or nonviable delivery (2; 1%); growth restriction or other condition of antepartum origin detected in the newborn (6; 3%); or failure to complete the protocol owing to scheduling difficulties, moving, and so forth (12; 6%). Eligibility for participation in the developmental follow-up was limited to the remaining 137 healthy offspring born at term of uncomplicated pregnancies and discharged from the newborn nursery on a routine schedule.

Ninety-four of the eligible participants who still lived in the area (76.4% compliance based on local availability; 68.6% of original sample) were tested at 24 months. The most common reason for lack of follow-up of the untested local families was inability of working parents to bring their child in for testing during the morning or early afternoon, which are the preferred times for developmental assessment. Sociodemographic characteristics of this group reflect a sample of mature (M maternal age = 32.0; SD = 3.6), well-educated (M years of maternal education = 17.0; SD = 2.0), married (95.7%), and nonminority (White, 85.1%; African American, 11.7%; Asian 3.2%) families. Child characteristics included normal birth weight (M = 3478.5 g; SD = 428), delivery close to 40 weeks gestation (M = 39.4 weeks; SD = 1.2), and normal 5-min Apgar scores (M = 9.0, SD = 0.4). Fifty-one percent were girls.

Maternal Psychological Measures

Maternal psychological assessments began mid-pregnancy and were administered at 24, 28, or 32 weeks gestation. The timing of the prenatal assessments was dependent upon the scheduling of fetal neurobehavioral and maternal physiological monitoring sessions of the parent study, the results of which are detailed elsewhere (DiPietro, Caulfield et al., 2004; DiPietro, Costigan, & Gurewitsch, 2005). The schedule of administration was designed to provide maximum breadth and depth of psychological measurement while minimizing participant burden and maintaining compliance. Participants were asked to complete the scales immediately before their scheduled visit. Two different scales were used to assess anxiety, stress, and depression. Pregnancy-specific experiences were assessed through a single scale. Assessments of maternal anxiety, stress, and depression were readministered at 6 weeks postpartum and again at 24 months, coincident with the child development assessment.

Anxiety. Maternal prenatal anxiety was assessed at 24 weeks gestation using the Anxiety subscale of the Profile of Moods Scale (POMS; McNair, Lorr, & Droppleman, 1971), a widely used measure of current emotional state. The original scale incorporated 65 adjectives (e.g., Discouraged, Cheerful) rated on 5-point scales from 0 (*not at all*) to 5 (*extremely*). Respondents are asked to report how they feel during the current day. Six subscales (depression, vigor, confusion, anxiety, anger, and fatigue) were derived. The current study used a shortened version of 37 adjectives that has been shown to preserve the reliability and subscale structure of the original (Shacham, 1983). The Anxiety subscale reflects the mean for six items (e.g., Tense, On edge). Anxiety was also assessed at 28 weeks gestation with the Spielberger State-Trait Anxiety Scales (STAI) (Spielberger, 1983). The STAI is among the most commonly used self-administered measures of anxiety and has been extensively validated. Anxiety is evaluated using twenty 4-point items; higher scores indicate higher anxiety. The State (Y-1) version of the scale was used in the current analysis (e.g., "I feel upset," "I am worried"). Postnatal anxiety was assessed at both 6 weeks and 24 months using the STAI.

Stress. Nonpregnancy-specific stress was assessed by the Daily Stress Inventory (DSI; Brantley, Waggoner, Jones, & Rappaport, 1987) at 24 weeks gestation. The DSI lists 58 potential sources of stress that may have been experienced in the last 24 hr (e.g., "Spoke in public," "Had car trouble"), each scored on a 7-point scale of stressfulness. The DSI yields an intensity measure (sum of scores divided by the number of nominated items), with higher scores indicating higher perceived stress. The scale has good psychometric properties (Brantley et al., 1987) and has been validated against measures of autonomic responsiveness and somaticism (Waters, Rubman, & Hurry, 1993). Stress was also measured at 28 weeks gestation with the Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983). Fourteen items are rated on a 5-point (0–4) scale to assess how stressful life has been during a specified period; in this case the questions were framed as "Since you became pregnant how often have you . . . ." Examples include ". . . found that you could not cope with all the things you had to do"; ". . . felt nervous and stressed." Postnatal stress was assessed using the PSS.

Depression. Depressed mood was assessed at 24 weeks gestation with the Depression subscale of the shortened POMS (McNair et al., 1971; Shacham, 1983). The subscale includes mean values for eight adjectives (e.g., Miserable, Hopeless). The second measure of depression was the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) administered at 32 weeks. The CES–D includes 20 depressive symptoms evaluated along 4-point (0–3) scales (e.g., I felt depressed, I had crying spells) reported for the period of the prior week. It has been widely applied during pregnancy and has an extensive validity and reliability history. Postnatal depressive symptomology was also assessed with the CES-D.

Pregnancy-specific stress. Pregnancy-specific hassles and uplifts were assessed by the Pregnancy Experience Scale (PES; DiPietro, Ghera, Costigan, & Hawkins, 2004). This scale was developed to measure maternal appraisal of exposures to daily, ongoing hassles and uplifts specific to pregnancy and contains 41 items (e.g., "Clothes and shoes don't fit," "How much the baby is moving," "Making nursery arrangements"). The PES structure was modeled on the nonpregnancy Hassles and Uplifts Scale (DeLongis, Folkman, & Lazarus, 1988). Respondents indicate the degree to which each item has made them feel "happy, positive, or uplifted" and "unhappy, negative or upset" on 4-point scales ranging from 0 (*not at all*) to 3 (*a great deal*). The scale has high internal reliability ($\alpha = .91-.95$) and both convergent and discriminant validity with existing measures of general affective intensity, anxiety, stress, and depression (DiPietro, Ghera et al., 2004). Scoring for this analysis was based on intensity values (i.e., sum of scores divided by the number of endorsed items) for both hassles (PES Hassles) and uplifts (PES Uplifts). The PES was administered at 32 weeks gestation.

Child Assessment

Child development was evaluated shortly after offspring reached their second birthday (*M* age = 24.8 months, *SD* = 0.9) using the Bayley Scales of Infant Development II (BSID), the most widely used and validated assessment of child development. The BSID generates two standardized scores: an MDI and a PDI. Testing was carried out by a clinical psychologist who was blind to maternal prenatal and postnatal psychological status.

The third BSID scale, the Infant Behavior Record (IBR), was also scored. For this age group, the scale consists of 26 items that are reduced to three factors that describe child behavior during the test situation. These include the degree to which children exhibit the following: (1) positive affect, initiative toward materials, lack of fearfulness, and social engagement with the tester (IBR-Orientation/Engagement); (2) attention and persistence toward tasks, cooperation, and good adaptation to new materials (IBR-Emotional Regulation); and (3) mature quality of motor behavior characterized by normal tone, fine and gross motor proficiency during tasks, and appropriate motor speed (IBR-Motor Quality). Items were dually scored by the examiner and an observer (interobserver reliability κs ranged from .82 to .85).

Before developmental assessment, baseline heart rate data were collected with three electrodes triangulated on the child's torso. Children were seated on their mothers' laps at a table and were shown a book or toy to minimize motor activity and distract them from the monitoring process. The signal was amplified (Physiocontrol, Plainview, NY) and digitized at 1,000 Hz. Data were manually edited for artifact and variables were quantified using MXedit software (Delta Biometrics, Bethesda, MD). Interbeat intervals (i.e., heart period) were computed (ms). The amplitude of the respiratory sinus arrhythmia, used as the index of vagal tone, was computed using methods developed by Porges (1985). Quantification proceeded through a series of filtering and detrending techniques to isolate the variance of heart period within the frequency band of spontaneous respiration. Extraction of high-frequency oscillations in heart period associated with respiration provides estimation of the parasympathetic influence on heart period as mediated by the sino-atrial node (Bar-Haim, Marshall, & Fox, 2000; Berntson et al., 1993). Heart period and vagal tone data were quantified in 30-s epochs and averaged over the recording.

Data Analysis

Exploratory data analysis included examination of variables for normalcy and outliers. Potential biasing of the sample of participants who did not engage in the follow-up was examined with *t* or Mann–Whitney *U* tests, depending on group size. Unadjusted associations between dependent and independent measures were evaluated using correlations. A series of regression analyses were designed to examine the predictive relations between prenatal psychological constructs and developmental measures. To provide the most conservative test that associations might be attributable to the prenatal and not the postnatal period, variables were entered in three hierarchical stages. Changes in R^2 at each subsequent stage were identified by *F* values. Sociodemographic covariates entered first into the equation were maternal education and fetal sex. Antecedent (6 week) and concurrent (24 month) psychosocial indicators were included at the second stage, and prenatal measures were entered at the final level. Both linear and curvilinear associations were tested. Fetal sex was examined as a moderator of potential associations by incorporating an interaction term (sex by each psychological variable) into analyses of variance.

Table 1
Descriptive Values for Maternal Psychological Measures

	All participants			Followed participants		
Measures	*M*	*SD*	*n*	*M*	*SD*	*n*
Prenatal						
POMS Anxiety	0.71	0.67	137	0.71	0.69	94
STAI Anxiety	35.80	10.26	137	35.44	10.27	94
DSI Stress	2.82	0.92	137	2.91	0.87	94
PSS Stress	22.70	8.08	136	22.59	8.54	93
POMS Depression	0.29	0.40	137	0.30	0.41	94
CES–D Depression	11.32	7.55	136	11.23	7.37	93
PES Hassles	1.43	0.27	136	1.43	0.29	93
PES Uplifts	1.91	0.42	136	1.90	0.43	93
6 weeks						
STAI anxiety	33.79	10.72	120	34.31	11.66	89
PSS Stress	23.30	7.30	119	23.65	7.44	88
CES–D Depression	11.11	8.13	119	11.53	8.60	88
24 months						
STAI Anxiety	—	—	—	32.60	9.11	86
PSS Stress	—	—	—	21.30	7.54	86
CES–D Depression	—	—	—	9.77	7.22	86

POMS = Profile of Mood Scale; STAI = Spielberger State Anxiety Scale; DSI = Daily Stress Inventory; PSS = Perceived Stress Scale; CES–D = Center for Epidemiological Studies Depression Scale; PES = Pregnancy Experience Scale.

Results

Mothers who participated in the follow-up were somewhat older ($M = 31.80$ vs. 30.0 years), $t(135) = 2.42$, $p < 0.05$, and more educated ($M = 17.0$ vs. 16.0 years), $t(135) = 2.42$, $p < 0.05$, than those who did not participate. There were no differences, however, between women who did and did not participate in the follow-up on any prenatal psychological measure.

Psychological Measures

Mean and standard deviations for all psychosocial variables are presented in Table 1. The first column represents values for the entire sample; the second for only those participants who took part in the 24-month follow-up. Slight variation in *n*s within assessment periods reflects instances of incomplete responses on specific scales.

Child Outcome Measures

Descriptive information for child variables is presented in Table 2. Bayley MDI and PDI scores could not be computed for a subset of children who were either too shy ($n = 2$) or noncompliant ($n = 8$). Two exams were not completed owing to examiner unavailability, resulting in a total of 82 participants with MDI and PDI values. The shy/noncompliant group did not significantly differ on any prenatal maternal psychological measure. Enough of the test was administered to allow scoring of the IBR, which assesses the child response to the test situation, for 8 ($n = 90$) of these children. Average MDI and PDI values were near the expected mean of 100. Mean scores for each behavioral factor fell between the 51st and 66th percentiles for this age.

Associations Between Prenatal Psychological Measures and Child Developmental Status

Table 3 presents the unadjusted correlations between prenatal psychological measures and Bayley MDI, PDI, and IBR scores. Positive, significant associations were detected between MDI and PDI scores and both the Anxiety and Depression subscales of the POMS. Nonpregnancy-specific stress as measured by the DSI was significantly associated with MDI scores. The patterning of associations for the two pregnancy-specific measures differed from the other measures. Pregnancy-specific hassles (PES Hassles) was the only measure to have a significant, but negative association with MDI, and pregnancy-specific uplifts (PES Uplifts) was the only measure to yield a significant, positive association with the IBR-Engagement/Orientation and IBR-Emotional Regulation scales.

Table 2
Child Development Measures at 24 Months

Measures	*M*	*SD*	*n*
Bayley II scale scores			
Mental Development Index (MDI)	102.00	13.23	82
Psychomotor Development Index (PDI)	96.55	12.08	82
Infant Behavior Record (IBR)			
Orientation/Engagement	35.73	5.57	90
Emotional Regulation	42.73	5.60	90
Motor Quality	37.99	2.21	90
Cardiac patterns			
Heart period (ms)	491.61	38.67	79
Vagal tone	4.27	1.02	79

Numerous factors can interfere with accurate developmental testing of young children, including fatigue and distractions. A total of 54 test sessions were identified in which the Bayley Scales were administered under ideal conditions. This excludes test sessions in which one of the following was present: the child was rated by the examiner as requiring significant coaxing to complete the assessment because they were either too fussy or shy; child fatigue due to approaching naptime or evening testing; maternal report and/or observation that the child wasn't feeling well; or the presence of siblings or other family members that provided a distraction. The magnitude of the correlations tended to increase when analysis was conducted on this subset of children. For example, the association between POMS Anxiety and MDI increases from $r=.29$ to $r=.36$, and the relation between PES Hassles and MDI increases from $r=-.27$ to $r=-.37$. The strengthening of the associations with the diminution of noise offers additional confidence that temperamental characteristics were not confounding observed results.

Regressions were conducted to evaluate potential predictive associations controlling for postnatal exposure. Measures of similar constructs during the prenatal period were aggregated to increase the stability of their estimates. Values for each assessment were *Z*-scored and combined into single values for prenatal anxiety (POMS Anxiety and STAI), stress (DSI and PSS), and depression (POMS Depression and CES-D). We refer to these as the prenatal anxiety, stress, and depression composites, respectively. The PES was collapsed into a ratio score

Table 3
Unadjusted Associations Between Prenatal Maternal Psychological and Child Development Measures

			Infant Behavior Record		
Measures	MDI	PDI	Engagement/Orientation	Emotional Regulation	Motor Quality
POMS Anxiety (24)[a]	.29**	.28**	.11	.13	.19[b]
STAI Anxiety (28)	.16	.21[b]	−.05	−.04	.18[b]
DSI Stress (24)	.22*	.12	.14	.09	.14
PSS Stress (28)	−.10	.19[b]	−.09	.00	.19[b]
POMS Depression (24)	.26*	.23*	.16	.12	.17
CES–D Depression (32)	.10	.17	.11	.09	.15
PES Hassles (32)	−.27*	−.04	−.05	.00	−.10
PES Uplifts (32)	−.07	.12	.22*	.22*	.13

[a]Denotes gestational week of administration.
[b]$p<.10$, *$p<.05$, **$p<.01$.
MDI = Mental Development Index; PDI = Psychomotor Development Index; POMS = Profile of Mood Scale; STAI = Spielberger State Anxiety Scale; DSI = Daily Stress Inventory; PSS = Perceived Stress Scale; CES – D = Center for Epidemiological Studies Depression Scale; PES = Pregnancy Experience Scale.

Table 4
Prediction of 2-Year Bayley Scale Scores From Prenatal Maternal Anxiety Composite

	Maternal Anxiety Composite							
	Mental Development Index (MDI)				Psychomotor Development Index (PDI)			
	β	*t*	*p*	Multiple *R*	β	*t*	*p*	Multiple *R*
Constant	88.73				99.09			
Maternal education	0.95	1.35	*ns*		− 0.08	− 0.12	*ns*	
Infant sex	3.97	1.36	*ns*	.24	4.01	1.48	*ns*	.18
		$R^2 = .059$; $F(2,74) = 2.34$				$R^2 = .034$; $F(2,74) = 1.29$		
6-week postnatal anxiety	− 0.15	− 0.92	*ns*		− 0.03	− 0.23	*ns*	
24 month postnatal anxiety	0.01	0.07	*ns*	.27	− 0.06	− 0.36	*ns*	.22
		$\Delta R^2 = .013$; $F(4,72) = 0.49$				$\Delta R^2 = .016$; $F(4,72) = 0.59$		
Prenatal anxiety composite	2.59	2.31	$< .05$	.37	2.40	2.32	$< .05$	.34
		$\Delta R^2 = .066$; $F(5,71) = 5.35$, $p < .05$				$\Delta R^2 = .067$; $F(5,71) = 5.36$, $p < .05$		

Table 5
Prediction of 2-Year Bayley Scale Scores From Prenatal Maternal Perceived Stress Composite

	Maternal Stress Composite							
	Mental Development Index (MDI)				Psychomotor Development Index (PDI)			
	β	*t*	*p*	Multiple *R*	β	*t*	*p*	Multiple *R*
Constant	81.81				103.00			
Maternal education	1.04	1.44	*ns*		− 0.20	− 0.31	*ns*	
Infant sex	4.52	1.49	*ns*	.24	4.36	1.62	*ns*	.18
		$R^2 = .059$; $F(2,74) = 2.32$				$R^2 = .034$; $F(2,74) = 1.29$		
6 week postnatal stress	− 0.07	− 0.27	*ns*		0.14	0.65	*ns*	
24 month postnatal stress	0.10	0.41	*ns*	.25	− 0.40	− 1.88	*ns*	.24
		$\Delta R^2 = .003$; $F(4,72) = 0.10$				$\Delta R^2 = .026$; $F(4,72) = 0.99$		
Prenatal stress composite	0.31	0.30	*ns*	.25	1.96	2.11	$< .05$	.34
		$\Delta R^2 = .001$; $F(5,71) = 0.09$				$\Delta R^2 = .055$; $F(5,71) = 4.43$, $p < .05$		

by dividing hassles intensity (PES Hassles) by uplift intensity (PES Uplifts), yielding a composite score of the degree of negative emotional valence exhibited toward the pregnancy. We refer to this new score as pregnancy-specific stress composite. Maternal education and infant sex were entered first into each equation.

Pearson correlation coefficients indicated no significant or near significant associations between any prenatal psychological measure and either infant birth weight or gestational duration (*r*s ranged from − 0.11 to 0.13); these were not included as potential confounding variables. Postnatal measures of each construct were included next, followed by the prenatal maternal measure. Tables 4–7 present the MDI and PDI results for each psychological construct. Individual beta weights, *t* values, and significance levels represent values when all variables are entered into the equation. *F* values test whether entry of each level (i.e., demographic, postnatal, prenatal) adds significant unique variance to the model. The change in R^2, on which this *F* is based, is also included. Regressions in each table are based on 76 subjects; variation in *n*s from earlier tables is a result of missing values for one or more components of the composite or covariate scores.

Neither maternal education, infant sex, nor any postnatal psychological measure contributed significant variance to MDI or PDI scores. Both the prenatal maternal anxiety composite (Table 4) and depression composite (Table 6) were significantly and positively associated with both MDI and PDI scores. Their

Table 6

Prediction of 2-Year Bayley Scale Scores From Prenatal Maternal Depression Composite

	Maternal Depression Composite							
	Mental Development Index (MDI)				Psychomotor Development Index (PDI)			
	β	*t*	*p*	Multiple *R*	β	*t*	*p*	Multiple *R*
Constant	84.13				93.69			
Maternal education	1.14	1.64	*ns*		0.16	0.25	*ns*	
Infant sex	3.52	1.14	*ns*	.24	3.56	1.29	*ns*	.18
	$R^2 = .059$; $F(2,74) = 2.34$				$R^2 = .034$; $F(2,74) = 1.29$			
6-week postnatal depression	− 0.17	− 0.84	*ns*		− 0.10	− 0.52	*ns*	
24-month postnatal depression	− 0.10	− 0.44	*ns*	.25	− 0.06	− 0.28	*ns*	.19
	$\Delta R^2 = .001$; $F(4,72) = 0.04$				$\Delta R^2 = .002$; $F(4,72) = 0.07$			
Prenatal depression composite	2.46	2.36	$p < .05$	.36	2.05	2.11	p < .05	.30
	$\Delta R^2 = .068$; $F(5,71) = 5.58$, $p < .05$				$\Delta R^2 = .057$; $F(5,71) = 4.47$, $p < .05$			

Table 7

Prediction of 2-Year Bayley Scale Scores From Prenatal Maternal Pregnancy Stress Composite

	Maternal Pregnancy Stress Composite							
	Mental Development Index (MDI)				Psychomotor Development Index (PDI)			
	β	*t*	*p*	Multiple *R*	β	*t*	*p*	Multiple *R*
Constant	85.90				102.70			
Maternal education	1.14	1.61	*ns*		0.02	0.03	*ns*	
Infant sex	4.74	1.59	*ns*	.24	4.780	1.78	*ns*	.18
	$R^2 = .059$; $F(2,74) = 2.34$				$R^2 = .034$; $F(2,74) = 1.29$			
6-week postnatal stress	0.07	0.28	*ns*		0.37	1.70	*ns*	
24-month postnatal stress	0.11	0.50	*ns*	.25	− 0.28	− 1.37	*ns*	.24
	$\Delta R^2 = .003$; $F(4,72) = 0.13$				$\Delta R^2 = .026$; $F(4,72) = 0.99$			
Pregnancy stress composite	− 12.00	− 1.57	*ns*	.31	− 14.89	− 2.17	p < .05	.34
	$\Delta R^2 = .032$; $F(5,71) = 2.47$				$\Delta R^2 = .058$; $F(5,71) = 4.69$, $p < .05$			

inclusion on the level of entry contributed an additional 5.7–6.8% unique variance after controlling for covariates. The prenatal perceived stress composite was unrelated to MDI but was significantly predictive of PDI (Table 5). Regressions conducted for the IBR-Engagement/Orientation and IBR-Emotional Regulation temperament factors (not shown; *n*s = 83 for these regressions) failed to detect significance for anxiety, stress, or depression composites (*p*s > .10). Both the anxiety, $R^2\Delta = .053$, $F(5,77) = 4.50$, $p < .05$, and stress composites, $R^2\Delta = .047$, $F(5,77) = 3.94$, $p < .05$, were positively and significantly predictive of IBR-Motor Quality after controlling for covariates.

Analyses for the composite PES score revealed a different pattern of results. Because there was no comparable postnatal measure to pregnancy-specific stress, the PSS was used as the postnatal control at 6 weeks and 24 months. The PES composite did not predict MDI scores, but was negatively associated with PDI (Table 7) and IBR-Motor Quality scores, $R^2\Delta = .050$, $F(5,77) = 4.22$, $p < .05$. In addition, greater tendency to perceive the pregnancy as more of a hassle than an uplift (i.e., PES composite) was associated with poorer IBR-Engagement/Orientation, $R^2\Delta = .072$, $F(5,78) = 6.23$, $p < .05$, and a trend towards lesser IBR-Emotional Regulation, $R^2\Delta = .039$, $F(5,78) = 3.51$, $p = .06$.

Behavior characterized by hyperactivity has been of special focus in some existing studies in this area. Separate analyses were conducted on an IBR item that is subsumed in the IBR-Emotional Regulation factor. This item measures fidgety and agitated

Table 8
Associations Between Individual Prenatal Maternal Psychological Measures and Child Cardiac Patterns (n's = 83 or 84)

	Heart period	Vagal tone
Psychological measure		
POMS Anxiety	.07	– .02
STAI Anxiety	– .18	– .15
DSI Stress	.03	– .06
PSS Stress	– .21[a]	– .22*
POMS Depression	.06	.02
CES – D Depression	– .23*	– .10
PES Hassles	– .25*	– .19[a]
PES Uplifts	– .05	– .15

[a]$p < .10$, *$p < .05$.
POMS = Profile of Mood Scale; STAI = Spielberger State Anxiety Scale; DSI = Daily Stress Inventory; PSS = Perceived Stress Scale; CES – D = Center for Epidemiological Studies Depression Scale; PES = Pregnancy Experience Scale.

motor activity during the attentional tasks. No child scored above a value of 3 (hyperactive during half of the assessment). Therefore, children were collapsed into two groups: those exhibiting no signs of this behavior ($n = 80$) versus those exhibiting some ($n = 14$). t tests detected no differences in any prenatal maternal measure between these groups.

No significant interactions between infant sex and maternal psychological variables were detected for MDI, PDI, or IBR scores. No significant curvilinear associations were found.

Associations Between Prenatal Psychosocial Measures and Child Cardiac Patterning

Seven children would not comply with electrode placement for heart rate recording, data from five children were of insufficient quality, and there were three instances of technical failure resulting in a total of 79 recordings (M recording duration = 7.6 min, $SD = 1.5$). Heart period (HP) and vagal tone values (Table 2) were within expected ranges (Bar-Haim et al., 2000) for this age group. The correlation between the cardiac measures was $r(77) = .66$, $p < .0001$. Boys displayed significantly longer HP than girls ($M = 502$ vs. 483 ms), $t(77) = 2.32$, $p < .05$, but there were no differences in vagal tone. Table 8 presents unadjusted correlations between cardiac measures and individual maternal psychological variables; the pattern of results for the two measures was relatively similar. As shown, the offspring of women with greater pregnancy-specific hassles (PES Hassles), depressive symptoms (CES-D), and, to a lesser degree, perceived stress (PSS) had significantly faster heart rates (i.e., shorter heart periods). Vagal tone was significantly associated only with PSS scores. However, when infant sex is included in regression equations for each of the psychosocial variables, all cardiac associations revert to or remain at only a trend level ($p < .10$) of significance. The composite stress, depression, anxiety, and pregnancy-specific stress scores used in the Bayley Scales regressions were not significantly correlated with either HP or vagal tone.

Discussion

The participants in this study were well-nourished, financially stable women with wanted pregnancies who were not subjected to traumatic events during pregnancy nor displayed clinical levels of anxiety or depression. As such, these findings may not generalize to stressors in the external environment that may generate either more intense or prolonged physiological responses or to clinical populations of anxious or depressed women at the upper extreme of these continua. Later in this discussion we consider the manner in which these sample characteristics may support a curvilinear association between prenatal distress and outcome (Huether, 1998). Moreover, because the psychological measures were not implemented until the second half of pregnancy, we may have missed detecting first trimester effects that have been implicated as more potent for outcomes than later exposure, although research findings have been inconsistent in this regard (Van den Bergh, Mulder et al., 2005).

Nonetheless, these findings do not support the notion that maternal anxiety, depression, or nonspecific stress during pregnancy within normal limits poses a significant threat to early child development or behavioral regulation. In contrast, we find modest, although consistent, support that these aspects of maternal psychological functioning are associated with more optimal early child development. However, the beneficial effects attributable to prenatal psychological factors, when detected, were small, ranging from only 5.5 – 6.8% of the variance. In addition, we found no evidence that nonpregnancy-specific distress (i.e., stress, anxiety or depression) interferes with temperamental attributes related to attentional capacity or emotional regulation. Our findings may provide relief to those concerned about the psychological implications for pregnant women of yet another pregnancy threat, in this case, causing women to worry about worrying (Oates, 2002).

The exception to this conclusion involves pregnancy-specific negativity. Children of women who appraised their pregnancy as more negative than positive showed slower psychomotor development and poorer emotional and attentional regulation during testing. The unique contribution of this measure to outcomes was also small (3.9–7.2% of the variance), and there is no obvious physiological mechanism through which pregnancy-specific stress should show associations in the opposite direction of measures of nonspecific stress. An obvious possibility is that this prenatal measure serves as a marker for characteristics of subsequent maternal–child interactions. That is, women who regard their pregnancy more negatively may be less likely to interact with their child in ways that foster development and socioemotional regulation. Our reliance on a nonspecific stress measure (i.e., the Perceived Stress Scale) as a postnatal variable in these equations may have resulted in insufficient control for such mediating facets of caregiving behavior. Partial support is provided by the finding that positive, uplifted feelings about pregnancy were positively related to child emotional and behavioral regulation scores (Table 3). However, the current results are consistent in direction and magnitude with those reported for a pregnancy-specific anxiety measure also administered near the same period of pregnancy (Buitelaar et al., 2003). In addition, an earlier report of a different sample isolated this particular indicator of the emotional valence toward pregnancy as more highly associated with alterations to fetal motor activity than with measures not specific to pregnancy (DiPietro, Hilton, Hawkins, Costigan, & Pressman, 2002). Pregnancy-specific stress is a relatively underrecognized and investigated source of maternal distress. Significant negativity toward the pregnancy may be an indicator of maternal behavioral or physiological pathways that exert an influence on the fetus in ways that are as yet unidentified.

With respect to autonomic function, several significant, negative associations were detected between maternal psychological variables and cardiac measures. Children of women with more depressive symptoms and greater pregnancy-specific stress had shorter resting heart period (i.e., faster heart rates). Vagal tone was negatively associated with perceived stress. Associations were small in magnitude, with no correlation exceeding $r = -0.25$, and associations were not consistently detected even for measures of the same psychological constructs. However, examination of the pattern of correlations in Table 8 suggests stronger associations for those measures that tap more persistent maternal characteristics as compared to measures that are mood based or based on daily events.

On the surface, the finding that nonpregnancy-specific maternal distress accelerates, rather than retards, development contraverts the evidence based on animal studies that show negative consequences of prenatal stress for later learning and performance (Welberg & Seckl, 2001). How do we reconcile the current findings against these results? First of all, close examination of this literature reveals nonuniversality of significant findings in animal models and some reports of beneficial effects. For example, rats subjected to mild stress showed *better* spatial learning coupled with facilitated differentiation in neuronal morphology (Fujioka et al., 2001) and *more* exploratory behavior (Meek, Burda, & Paster, 2000). Repeated exposures to prenatal stress confer an adaptive or protective effect on postnatal reactivity in some groups of rodents (Van den Hove et al., 2005). Within the animal literature, one of the most consistent consequences of prenatal exposure to stress, altered gender-specific behavior in offspring (Ward & Stehm, 1991), has not been replicated in children (Hines et al., 2002). Issues of timing and severity of the prenatal stressors, as well as demand characteristics of the test, may be responsible for the disparity in findings within the animal literature. But perhaps most important to failure of the current study to detect a deleterious effect of stress is that the controlled experimental stress manipulations used in animal models may not provide an appropriate analogue to human studies.

As noted earlier, almost all human studies, including this one, rely on measurement of self-reported stress, anxiety, and depressive symptoms that likely reflect persistent maternal attributes and may not be closely related to the prevalence or severity of stressful events. In the single instance in which developmental outcomes were followed after a natural emergency (Laplante et al., 2004), maternal perceptions of the stressfulness of the event were unrelated to child outcomes; instead, the magnitude of actual disruption to daily life as a result of the emergency was the significant predictor (Laplante et al., 2004). Thus we believe that the data generated by both rodent and nonhuman primate models regarding stress effects on offspring do not provide parallel to studies that measure maternal psychological characteristics.

The specific mechanism by which maternal psychological distress is transduced to the fetus in order to incur beneficial or deleterious effects is unknown. The most commonly discussed involve consequences of activation of the HPA and sympathetic-adrenomedullary (SAM) axes. Fetal effects may be generated by placental transfer of glucocorticoids or neurotransmitters with resultant alterations to regulatory feedback systems that may have consequences for specific brain regions (Kaiser & Sachser, 2005; Mulder et al., 2002). Maternal cortisol levels are significantly ($r = .60$) correlated with fetal levels, although the fetal concentrations are lower (Gitau, Cameron, Fisk, & Glover, 1998). A report based on a small sample ($n = 17$) found that higher maternal cortisol levels late in gestation corresponded to observational measures of child fussiness and negativity in the first months of life (de Weerth, van Hees, & Buitelaar, 2003). Activation of the SAM system has well-known constrictive effects on maternal vasculature and may produce chronic or episodic hypoxia in the fetus as a result of impairment to uteroplacental blood flow (Morishima, Pedersen, & Finster, 1978; Myers, 1975). There is evidence that maternal trait anxiety is associated with alterations in blood flow in the umbilical and fetal middle cerebral arteries (Sjostrom, Valentin, Thelin, & Marsal, 1997). No current model sufficiently distinguishes between potential mechanisms that may differentiate effects of maternal anxiety, depression, or stress on the developing fetus.

Curiously absent from the discourse on the relation between prenatal distress and outcomes has been the long-standing observation that mild stress accelerates growth and development. Early observations noted positive relations between mild perinatal hypoxia and physical development in early childhood (Graham, Caldwell, Ernhart, Pennoyer, & Hartman, 1957). Physiological stress associated with intrauterine conditions such as maternal hypertension and growth restriction has a well-known acceleratory effect on both organ development and neuromaturation (Allen & Donohue, 2002). Consistent with this is an observation of better Apgar scores in neonates of women with greater negative emotionality during pregnancy (Ponirakis et al., 1998). The fetus responds to hypoxic threats, such as cord compression or maternal hypoxia, by increasing the volume of blood directed to the brain, heart, and adrenals above that of nonstress conditions (Thornburg, 1991). Supportive, although indirect, evidence of the beneficial effects of mild physiological stress can be found in a series of studies comparing matched groups of women who either continued to exercise during pregnancy or refrained from training. Offspring of the women who continued to exercise regularly displayed better neuromaturation at birth and intellectual functioning at age 5 (Clapp, 1996).

There are at least two distinct, although not incompatible, hypotheses that may explain our findings of acceleratory effects of prenatal maternal distress. Huether (1998) has proposed that the human postnatal brain requires sufficient, but not excessive, psychosocial stress to promote optimal synaptic structure. A similar model of moderate intrauterine exposure in the promotion of optimal adaptation has been put forth by Amiel-Tison et al. (2004). Both echo the classic inverted U-shaped function of the relation between arousal and performance (Yerkes & Dodson, 1908). Although we did not detect curvilinear associations in this study, this was a nonclinical sample and the upper threshold above which deleterious associations might emerge may not have been reached. However, the contrasting finding of lower MDI scores at the same age in an earlier report (Brouwers et al., 2001) may be consistent with this interpretation. Significant results were based on dichotomizing anxiety into high scores (>1 *SD* above mean) versus all others; a similar approach (upper 25th percentile) was necessitated in another study (Van den Bergh, Mennes et al., 2005). Descriptive values are not provided in the former but examination of those in the latter report reveals substantially higher mean STAI anxiety values than comparable ones in the current study providing potential support for curvilinear associations.

We propose a second, more speculative mechanism that may also explain how moderate prenatal anxiety or stress can have positive consequences for offspring development. The intrauterine milieu presented to the fetus by distressed and nondistressed women may differ along "meta" continua of predictability and stimulation with implications for neural development. That is, more emotionally "charged" women may present more labile environments that include more frequent changes in sounds emanating from the maternal cardiovascular and gastrointestinal systems, variation in local thermodynamics, and other acoustic or somatosensory stimuli. Evidence for fetal responsiveness to intrauterine sensory changes is provided by the rapidity with which fetuses respond to experimentally induced maternal stress (DiPietro, Costigan, & Gurewitsch, 2003; Monk, Myers, Sloan, Ellman, & Fifer, 2003). These may provide additional levels of stimulation as well as rudimentary classical conditioning because many of these stimuli predictably precede and overlap with hormonal surges from the pregnant woman. Heightened opportunities for conditioning may, in turn, stimulate neural development (Novak, 2004), whereas excessive amounts of stimulation may overwhelm the response capabilities of the fetus.

The sociodemographic characteristics of the pregnant women in most of the studies detailed in the introduction, which are predominantly of European origin (Huizink et al., 2002; Van den Bergh & Marcoen, 2004), are similar to those of the current sample and alone cannot explain observed differences in results. However, attention to the nature of the psychological measures used in different cohorts is warranted. For example, the pregnancy anxiety measure used in one of these longitudinal samples includes two nonstandard subscales described as "fear of giving birth to a handicapped child" (four items) and "fear of giving birth" (three items). Some results are based on a combined score (Huizink et al., 2002), whereas others are based on only one of these (Gutteling et al., 2005). The specificity of the constructs assessed in these may vary across locales based on cultural influences on the pregnancy experience. Differences in the nuances of maternal psychological profiles and measures across samples, which may vary by characteristics of volunteer populations in different cultures, may contribute to the lack of comparable results.

The current findings support careful reconsideration of the existing notions of the consequences of maternal distress during pregnancy on child development. The results of this study support a downward extension to the fetal period of the notion commonly applied to postnatal performance and development that both too little and too much stress may be maladaptive, but moderate amounts can be facilitative.

References

Allen, M., & Donohue, P. (2002). Neuromaturation of multiples. *Seminars in Neonatology*, *7*, 211–221.

Amiel-Tison, C., Cabrol, D., Denver, R., Jarreau, P., Papiernik, E., & Piazza, P. (2004). Fetal adaptation to stress Part I: Acceleration of fetal maturation and earlier birth triggered by placental insufficiency in humans. *Early Human Development*, *78*, 15–27.

Arizmendi, T., & Affonso, D. (1987). Stressful events related to pregnancy and postpartum. *Journal of Psychosomatic Research*, *31*, 743–756.

Atella, L., DiPietro, J., Smith, B., & St. James-Roberts, I. (2003). More than meets the eye: Parental and infant contributors to maternal and paternal reports of early infant difficultness. *Parenting: Science and Practice*, *3*, 265–284.

Bar-Haim, Y., Marshall, P., & Fox, N. (2000). Developmental changes in heart period and high frequency heart period variability from 4 months to 4 years of age. *Developmental Psychobiology*, *37*, 44–56.

Berkowitz, G., Wolff, M., Janevic, T., Holzman, I., Yehuda, R., & Landrigan, P. (2003). The World Trade Center disaster and intrauterine growth restriction. *Journal of the American Medical Association*, *290*, 595–596.

Berntson, G., Cacioppo, J., & Quigley, K. (1993). Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology*, *30*, 183–196.

Brantley, P. J., Waggoner, C. D., Jones, G. N., & Rappaport, N. B. (1987). A daily stress inventory: Development, reliability, and validity. *Journal of Behavioral Medicine*, *10*, 61–73.

Brouwers, E., van Baar, A., & Pop, V. (2001). Maternal anxiety during pregnancy and subsequent infant development. *Infant Behavior & Development*, *24*, 95–106.

Buitelaar, J., Huizink, A., Mulder, E., Robles de Medina, P., & Visser, G. (2003). Prenatal stress and cognitive development and temperament in infants. *Neurobiology of Aging*, *24*, S53–S60.

Calkins, S., & Dedmon, S. (2000). Physiological and behavioral regulation in two-year-old children with aggressive/destructive behavior problems. *Journal of Abnormal Child Psychology*, *28*, 103–118.

Carlson, D., & LaBarba, R. (1979). Maternal emotionality during pregnancy and reproductive outcome: A review of the literature. *International Journal of Behavioral Development*, *2*, 343–376.

Clapp, J. (1996). Morphometric and neurodevelopmental outcome at age five years of the offspring of women who continued to exercise regularly throughout pregnancy. *Journal of Pediatrics*, *129*, 856–863.

Clarke, A. S., & Schneider, M. L. (1993). Prenatal stress has long-term effects on behavioral responses to stress in juvenile rhesus monkeys. *Developmental Psychobiology*, *26*, 293–304.

Clarke-Stewart, K., Fitzpatrick, M., Allhusen, V., & Goldberg, W. (2000). Measuring difficult temperament the easy way. *Developmental and Behavioral Pediatrics*, *21*, 207–223.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*, 385–396.

DaCosta, D., Brender, W., & Larouche, J. (1998). A prospective study of the impact of psychosocial and lifestyle variables on pregnancy complications. *Journal of Psychosomatic Obstetrics and Gynecology*, *19*, 28–37.

Davis, E., Snidman, N., Wadhwa, P., Glynn, L., Dunkel-Schetter, C., & Sandman, C. (2004). Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy*, *6*, 319–331.

DeLongis, A., Folkman, S., & Lazarus, R. S. (1988). The impact of daily stress on health and mood: Psychological and social resources as mediators. *Journal of Personality and Social Psychology*, *54*, 486–495.

de Weerth, C., van Hees, Y., & Buitelaar, J. (2003). Prenatal maternal cortisol levels and infant behavior during the first 5 months. *Early Human Development*, *74*, 139–151.

DiPietro, J., Caulfield, L., Costigan, K., Merialdi, M., Nguyen, R., Zavaleta, N., et al. (2004). Fetal neurobehavioral development: A tale of two cities. *Developmental Psychology*, *40*, 445–456.

DiPietro, J., Costigan, K., & Gurewitsch, E. (2003). Fetal response to induced maternal stress. *Early Human Development*, *74*, 125–138.

DiPietro, J., Costigan, K., & Gurewitsch, E. (2005). Maternal physiological change during the second half of gestation. *Biological Psychology, 69*, 23 – 38.

DiPietro, J., Ghera, M., Costigan, K., & Hawkins, M. (2004). Measuring the ups and downs of pregnancy. *Journal of Psychosomatic Obstetrics and Gynecology*, *25*, 189 – 201.

DiPietro, J., Hilton, S., Hawkins, M., Costigan, K., & Pressman, E. (2002). Maternal stress and affect influence fetal neurobehavioral development. *Developmental Psychology, 38*, 659 – 668.

Engel, S., Berkowitz, G., Wolff, M., & Yehuda, R. (2005). Psychological trauma associated with the World Trade Center attacks and its effect on pregnancy outcome. *Paediatric and Perinatal Epidemiology, 19*, 331 – 341.

Fameli, M., Kitraki, E., & Sylianopolou, F. (1994). Effects of the hyperactivity of the maternal hypothalamic-pituitary-adrenal axis during pregnancy on the development of the HPA axis and brain monoamines of the offspring. *International Journal of Developmental Neuroscience*, *12*, 651 – 659.

Fujioka, T., Fujioka, A., Tan, N., Chowdhury, G., Mouri, H., Sakata, Y., et al. (2001). Mild prenatal stress enhances learning performance in the non-adopted rat offspring. *Neuroscience*, *103*, 301 – 307.

Gitau, R., Cameron, A., Fisk, N., & Glover, V. (1998). Fetal exposure to maternal cortisol. *Lancet*, *352*, 707 – 708.

Glynn, L., Wadhwa, P., Dunkel-Schetter, C., Chicz-Demet, A., & Sandman, C. (2001). When stress happens matters: Effects of earthquake timing on stress responsivity in pregnancy. *American Journal of Obstetrics and Gynecology, 184*, 637 – 642.

Graham, F., Caldwell, B., Ernhart, C., Pennoyer, M., & Hartman, A. (1957). Anoxia as a significant perinatal experience: A critique. *Journal of Pediatrics*, *50*, 556 – 569.

Gutteling, B., de Weerth, C., Willemsen-Swinkels, S., Huizink, A., Mulder, E., Visser, G., et al. (2005). The effects of prenatal stress on temperament and problem behavior of 27-month-old toddlers. *European Child and Adolescent Psychiatry, 14*, 41 – 51.

Henry, C., Kabbaj, M., Simon, H., Moal, M. L., & Maccari, S. (1994). Prenatal stress increases the hypothalmic-pituitary-adrenal axis response in young and adult rats. *Journal of Neuroendocrinology, 6*, 341 – 345.

Hines, M., Johnston, K., Golombok, S., Rust, J., Stevens, M., & Golding, J. (2002). Prenatal stress and gender role behavior in girls and boys: A longitudinal, population study. *Hormones and Behavior, 42*, 126 – 134.

Holmes, T. H., & Rahe, R. H. (1967). The social readjustment rating scale. *Journal of Psychosomatic Research*, *11*, 213 – 218.

Huether, G. (1998). Stress and the adaptive self-organization of neuronal connectivity during early childhood. *International Journal of Neuroscience*, *16*, 297 – 306.

Huffman, L., Bryan, Y., del Carmen, R., Pedersen, F., Doussard-Roosevelt, J. A., & Porges, S. (1998). Infant temperament and cardiac vagal tone: Assessments at twelve weeks of age. *Child Development*, *69*, 624 – 635.

Huizink, A., Mulder, E., Robles de Medina, P., Visser, G., & Buitelaar, J. (2004). Is pregnancy anxiety a distinctive syndrome? *Early Human Development*, *79*, 81 – 91.

Huizink, A., Robles de Medina, P., Mulder, E., Visser, G., & Buitelaar, J. (2002). Psychological measures of prenatal stress as predictors of infant temperament. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*, 1078 – 1085.

Kaiser, S., & Sachser, N. (2005). The effects of prenatal social stress on behaviour: Mechanisms and functions. *Neuroscience and Biobehavioral Reviews*, *29*, 283 – 294.

Kofman, O. (2002). The role of prenatal stress in the etiology of developmental behavioral disorders. *Neuroscience and Biobehavioral Reviews*, *26*, 457 – 470.

Kumar, R., Robson, K. M., & Smith, A. M. R. (1984). Development of a self-administered questionnaire to measure maternal adjustment and maternal attitudes during pregnancy and after delivery. *Journal of Psychosomatic Research*, *28*, 43 – 51.

Laplante, D., Barr, R., Brunet, A., DuFort, G., Meaney, M., Saucier, J., et al. (2004). Stress during pregnancy affects general intellectual and language functioning in human toddlers. *Pediatric Research*, *56*, 400 – 410.

Lobel, M. (1994). Conceptualizations, measurement, and effects of prenatal maternal stress on birth outcomes. *Journal of Behavioral Medicine*, *17*, 225 – 272.

McNair, D., Lorr, M., & Droppleman, L. (1971). *Manual for the Profile of Mood States*. Educational and Industrial Testing Service, San Diego.

Mednick, B., Hocevar, D., & Baker, R. (1996). Personality and demographic characteristics of mothers and their temperament ratings of child difficultness. *International Journal of Behavioral Development*, *19*, 121 – 140.

Meek, L., Burda, K., & Paster, E. (2000). Effects of prenatal stress on development in mice: Maturation and learning. *Physiology and Behavior*, *71*, 543 – 549.

Monk, C., Myers, M., Sloan, R., Ellman, L., & Fifer, W. (2003). Effects of women's stress-elicited physiological activity and chronic anxiety on fetal heart rate. *Developmental and Behavioral Pediatrics*, *24*, 32 – 38.

Morishima, H., Pedersen, H., & Finster, M. (1978). The influence of maternal psychological stress on the fetus. *American Journal of Obstetrics and Gynecology, 131*, 286 – 290.

Mulder, E., Robles de Medina, P., Huizink, A., Van den Bergh, B., Buitelaar, J., & Visser, G. (2002). Prenatal maternal stress: Effects on pregnancy and the (unborn) child. *Early Human Development*, *70*, 3 – 14.

Myers, R. (1975). Maternal psychological stress and fetal asphyxia: A study in the monkey. *American Journal of Obstetrics and Gynecology, 122*, 47 – 59.

Novak, M. (2004). Fetal-maternal interactions: Prenatal psychobiological precursors to adaptive infant development. *Current Topics in Developmental Biology, 59*, 37 – 60.

Oates, M. (2002). Adverse effects of maternal antenatal anxiety on children: Causal effect or developmental continuum? *British Journal of Psychiatry*, *180*, 478 – 479.

O'Connor, T., Heron, J., Glover, V., & Team, A. S. (2002). Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 1470 – 1477.

O'Connor, T., Heron, J., Golding, J., Beveridge, M., & Glover, V. (2002). Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. *British Journal of Psychiatry*, *180*, 502 – 508.

Paarlberg, K. M., Vingerhoets, A., Passchier, J., Dekker, G., & van Geijn, H. (1995). Psychosocial factors and pregnancy outcome: A review with emphasis on methodological issues. *Journal of Psychosomatic Research*, *39*, 563 – 595.

Pauli-Pott, U., Ries-Hahn, A., Kupfer, J., & Beckmann, D. (1999). Covariation of parental judgments of child behavioral characteristics with a developmental scale and observation of behaviors. *Praxis der Kinderpsycholie und Kinderpsychiatrie (abstract in English)*, *48*, 311 – 325.

Ponirakis, A., Susman, E. J., & Stifter, C. A. (1998). Negative emotionality and cortisol during adolescent pregnancy and its effect on infant health and autonomic nervous system reactivity. *Developmental Psychobiology*, *33*, 163 – 174.

Porges, S. W. (1983). Heart rate patterns in neonates: A potential diagnostic window to the brain. In T. Field & A. Sostek (Eds.), *Infants born at risk: Physiological, perceptual, and cognitive processes* (pp. 3 – 22). New York: Grune & Stratton.

Porges, S. (1985). *Method and apparatus for evaluating rhythmic oscillations in aperiodic physiological response systems*. Washington DC: US Patent Office.

Porges, S. (1992). Vagal tone: A marker of stress vulnerability. *Pediatrics*, *90*, 498 – 504.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*, 385 – 401.

Schneider, M., & Moore, C. (2000). Effects of prenatal stress on development: A non-human primate model. In C. Nelson (Ed.), *The effects of early adversity on neurobehavioral development* (*Vol. 31*, pp. 201 – 244). Mahwah, NJ: Lawrence Erlbaum Associates.

Schneider, M., Moore, C., Kraemer, G., Roberts, A., & DeJesus, O. (2002). The impact of prenatal stress, fetal alcohol exposure, or on development: Perspectives from a primate model. *Psychoneuroendocrinology*, *27*, 285 – 298.

Schneider, M., Roughton, E., Koehler, A., & Lubach, G. (1999). Growth and development following prenatal stress exposure in primates: An examination of ontogenetic vulnerability. *Child Development*, *70*, 263 – 274.

Shacham, S. (1983). A shortened version of the Profile of Mood States. *Journal of Personality Assessment*, *47*, 305 – 306.

Sjostrom, K., Valentin, L., Thelin, T., & Marsal, K. (1997). Maternal anxiety in late pregnancy and fetal hemodynamics. *European Journal of Obstetrics and Gynecology*, *74*, 149 – 155.

Spielberger, C. (1983). *Manual for the State-Trait Anxiety Inventory (Form Y)*. Palo Alto, CA: Mind Garden Inc.

Thornburg, K. (1991). Fetal response to intrauterine stress. *Ciba Foundation Symposium*, *156*, 17 – 29.

Van den Bergh, B. (1990). The influence of maternal emotions during pregnancy on fetal and neonatal behavior. *Pre- and Peri-natal Psychology*, *5*, 119 – 130.

Van den Bergh, B., & Marcoen, A. (2004). High antenatal maternal anxiety is related to ADHD symptoms, externalizing problems, and anxiety in 8- and 9-year-olds. *Child Development*, *75*, 1085 – 1097.

Van den Bergh, B., Mennes, M., Oosterlaan, J., Stevens, V., Stiers, P., Marcoen, A., et al. (2005). High antenatal maternal anxiety is related to impulsivity during performance on cognitive tasks in 14- and 15-year-olds. *Neuroscience and Biobehavioral Reviews*, *29*, 259 – 269.

Van den Bergh, B., Mulder, E., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioral development of the fetus and child: Links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews*, *29*, 237 – 258.

Van den Hove, D., Blanco, C., Aendekerk, B., Desbonnet, L., Bruschettini, M., Steinbusch, H., et al. (2005). Prenatal restraint stress and long-term affective consequences. *Developmental Neuroscience*, *27*, 313 – 320.

Ward, I., & Stehm, K. (1991). Prenatal stress feminizes juvenile play patterns in male rats. *Physiology and Behavior*, *50*, 601 – 605.

Waters, W. F., Rubman, S., & Hurry, M. J. (1993). The prediction of somatic complaints using the Autonomic Nervous System Response Inventory and the Daily Stress Inventory. *Journal of Psychosomatic Research*, *37*, 117 – 126.

Weinstock, M. (2001). Alterations induced by gestational stress in brain morphology and behavior of the offspring. *Progress in Neurobiology*, *65*, 427 – 451.

Welberg, L., & Seckl, J. (2001). Prenatal stress, glucocorticoids and the programming of the brain. *Journal of Neuroendocrinology*, *13*, 113 – 128.

Yali, A., & Lobel, M. (1999). Coping and distress in pregnancy: An investigation of medically high risk women. *Journal of Psychosomatic Obstetrics and Gynecology*, *20*, 39 – 52.

Yerkes, R., & Dodson, J. (1908). The relation of strength of stimulus to rapidity of habit-formation. *Journal of Comparative Neurology and Psychology*, *18*, 450 – 482.

Zajicek, E., & Wolkind, S. (1978). Emotional difficulties in married women during and after the first pregnancy. *British Journal of Medical Psychology*, *51*, 379 – 385.