Maternal Panic Disorder: Infant Temperament, Neurophysiology, and Parenting Behaviors

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ABSTRACT

Objective: To determine whether 4- and 14-month-old infants of mothers with panic disorder (PD) would be more likely to show differences in temperament, neurophysiology (salivary cortisol and sleep), and relationships with their mothers than controls. **Method:** Two cohorts were recruited: 4-month-old infants with PD mothers ($n = 25$) and 4-month-old controls ($n = 24$), and 14-month-old infants with PD mothers ($n = 27$) and 14-month-old controls ($n = 18$). Mothers completed diagnostic interviews and questionnaires concerning infant temperament, sleep, and parenting. Infant salivary cortisol samples and standard observational procedures to measure infant temperament, sleep, attachment, and parenting were also used. **Results:** Infants with PD mothers did not show more high reactivity, behavioral inhibition, or ambivalent/resistant attachment but did demonstrate different neurophysiology (higher salivary cortisol and more disturbed sleep) than controls. PD mothers also displayed less sensitivity toward their infants and reported parenting behaviors concerning infant sleep and discipline that have been associated with child problems. **Conclusions:** While infants with PD mothers did not show early behavioral differences from controls, they did display neurophysiological divergences consistent with higher arousal/arousability. Such neurophysiological divergences (elevated salivary cortisol and disturbed sleep) might be important early indicators of risk. Helping PD mothers parent their more highly aroused/arousable infants could reduce the development of psychopathology. *J. Am. Acad. Child Adolesc. Psychiatry*, 2003, 42(7):814–825. **Key Words:** infant, panic disorder, temperament, neurophysiology, parenting.

Recent research has sought to elucidate the origins of anxiety disorders by studying children of parents with anxiety disorders, because such children have been shown to be at higher risk for anxiety disorders (Hettema et al., 2001; Weissman, 1988). Several studies have focused on children of parents with panic disorder (PD) because these children are at high risk for multiple anxiety disorders (Biederman et al., 1991, 2001a). Children with PD parents have been shown to be more likely than children of parents without psychopathology to have a temperament called behavioral inhibition (BI) (Rosenbaum et al., 1988, 2000), which has been found to predict later anxiety disorders (Biederman et al., 1993, 2001b; Schwartz et al., 1999). BI has generally been characterized as quiet withdrawal in response to novel inanimate stimuli and strangers (Kagan, 1994). Previous investigations concerning BI in children of parents with PD have focused primarily on 2- through 7-year-old children (Rosenbaum et al., 1988, 2000). No previous research has examined younger infants and toddlers of PD parents. Studies concerning early markers for BI in nonclinical samples have shown that 4-month-old infants who display "high reactivity" or high motor and cry activity in response to novel stimuli are more likely to manifest BI later (Fox et al., 2001; Kagan et al., 1998). If high reactivity and BI were found in young children of PD parents, this would suggest that high-risk children show indicators of risk for anxiety disorders very early in life. If high reactivity and BI were not

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identified in the young children, this could suggest that BI develops later, perhaps in response to parenting behaviors.

In addition to behavioral differences, children with anxious/PD parents show neurophysiological differences from controls, which could be indicative of increased arousal/arousability (Merikangas et al., 1999). Identifying neurophysiological risk indicators could also be beneficial because it would allow for the discovery of children likely to develop psychopathology and for the monitoring of changes in their risk status. One promising potential indicator that has been identified has involved the hypothalamic-pituitary-adrenal (HPA) axis and salivary cortisol responses. The HPA axis has been described as being activated often in association with conditions of fear, anxiety, or threat (Schulkin et al., 1994). Although elevations of salivary cortisol have not been consistently found in relation to anxiety disorders in older children and adults, possibly due to differences in context (Gunnar, 2001), studies have provided evidence that higher levels of salivary cortisol could be associated with risk for internalizing symptoms (Goldsmith and Lemery, 2000; Granger et al., 1994, 1998; Schmidt et al., 1997). Thus elevated salivary cortisol, which might be indicative of increased arousal/arousability, could be a potentially useful marker of early risk status.

A second domain of measures that could signify increased arousal/arousability and risk concerns the regulation of sleep or arousal patterns. Sleep and arousal have been conceptualized as closely associated, opponent processes (Dahl, 1996). Difficulties settling to sleep and with sleep continuity (the ability to sleep throughout the night) have been associated with increased arousal, fearfulness, and anxiety (Kazarian et al., 1978). Multiple studies have identified adults with PD as having difficulties with sleep continuity (Arriaga et al., 1996; Lauer et al., 1992; Stein et al., 1993). Merikangas and colleagues (1999) reported increased sleep terrors in 7- to 17-year-old children of parents with anxiety disorders/PD. Seifer and colleagues (1996) found sleep disturbances in young children to be associated with both maternal psychopathology and child internalizing symptoms. Thus young children with sleep disturbances could be showing increased difficulties with arousal/arousability and could be at greater risk for psychopathology.

Parenting behaviors, such as more maternal feedings at night, not putting the children to bed awake, and sleeping with the children, also contribute to infant sleep difficulties (Wolfson et al., 1992) and could be more common in anxious parents. Several researchers have furthermore described anxious parents as displaying other behaviors that could play a role in the development of anxiety disorders (Dadds and Roth, 2001; Manassis, 2001). Factor analytic studies have identified two important dimensions of parenting behaviors: (1) parental warmth/sensitivity and (2) parental control and disciplinary behaviors (Rapee, 1997). Less sensitive parenting behaviors have been identified as likely to contribute to anxiety disorders because such behaviors have been associated with insecure attachment relationships (Ainsworth et al., 1978), which increase the risk for later anxiety disorders (Warren et al., 1997). Children with anxious/PD mothers have been seen to have high levels of insecure attachment (Manassis et al., 1994), and anxious/PD mothers have been shown to be less warm and positive and more critical and intrusive with their children than controls (Weinberg and Tronick, 1998; Whaley et al., 1999). Little research has examined the behaviors of PD mothers toward younger children, before the children have developed clear psychopathology. Moreover, little research has examined the control and disciplinary behaviors of anxious mothers, especially during the emergence of child independence (toddlerhood).

This investigation was conducted to fill these important research gaps by examining infant temperament, neurophysiology, parenting behaviors, and infant–parent attachment relationships for extremely young infants with PD mothers. Infants with PD mothers were hypothesized to display more high reactivity and BI in response to inanimate novel stimuli and strangers compared with controls. Infants with PD mothers were also hypothesized to have higher salivary cortisol levels, more trouble settling to sleep, decreased sleep continuity, and more sleep disorders than controls. In addition, PD mothers were expected to show parenting behaviors associated with more disturbed infant sleep (more maternal feedings at night, not putting the children to bed awake, and sleeping with the children), less sensitivity, and less effective parenting behaviors in disciplinary situations with their children than controls. Infants with PD mothers were predicted to have more ambivalent/resistant and disorganized insecure attachment relationships than controls because ambivalent/resistant attachment had been found to predict later anxiety disorders (Warren et al., 1997) and because infants could develop disorganized attachment as a result of seeing their mothers repeatedly experience panic (Main and Hesse, 1990). Clarifying whether these temperament, neurophysiology, parenting, and relationship differences are seen in early childhood could suggest directions for the development of preventive interventions for anxiety disorders.

METHOD

Participants

All subjects were recruited from the same two sources: the Institute of Child Development in Minnesota and through advertising for mothers with panic attacks. The Institute of Child Development compiles lists of volunteers by mailing information to parents of all newborns born within the surrounding vicinity. Parents who respond are then contacted and asked about participation in particular studies. In this case, parents were contacted prior to the required ages and were screened using the Structured Clinical Interview for *DSM-IV* (SCID) screener (First et al., 1996). Mothers were interviewed if they reported having panic attacks or no symptoms. Families were excluded if the child was identified as having experienced a major medical problem, trauma, or abuse or if the parent had abused drugs or alcohol during the pregnancy or child's lifetime because these factors could confound the results (Hill et al., 1999; Malmquist, 1986; Terr, 1981). In contrast, alcohol abuse/dependence that had ended prior to the pregnancy was not an exclusionary criterion for either group. Of the parents who were contacted, approximately 37% refused participation because of lack of time and an additional 14% were ineligible. The human subjects institutional review board approved the study, and all parents signed informed consent documents after being fully informed about the study procedures.

Eighty-seven children (43 boys and 44 girls) were recruited to participate in two different cohorts. Families with 4- and 14-month-old children were studied because those are the ages for which the temperament procedures had been validated (Kagan, 1994). For the 4-month cohort (recruited for temperament procedures done between 3.5 and 4.5 months), 25 infants had mothers with PD and 24 had mothers without psychopathology. For the 14-month cohort (recruited for temperament procedures done between 13 and 15 months), 27 infants had mothers with PD and 18 had mothers without psychopathology. Seven infants (four with PD mothers) participated at least partially in both cohorts. In addition, infants in the 14-month cohort participated in a second laboratory visit when they were approximately 15 months of age. Because the testing extended over several years and because this second laboratory visit could also be conducted with 1-year-old infants as well as with 15-month-old infants, some of the infants in the 4-month cohort who reached 1 year of age within the course of the study (n = 27) were also able to participate in this laboratory visit, resulting in a sample of 36 infants with PD mothers and 35 controls for the Strange Situation Procedure (SSP) (mean age = 15.2, SD = 1.6) that is described below.

Mothers averaged 31 years of age (SD = 4.2) and were white except for one African American and one American Indian/Alaskan Native. One mother was Hispanic. Socioeconomic status assessed with the Hollingshead Four-Factor Index (Hollingshead, 1975) showed that the majority of families (83%) were in the two highest levels (e.g., "business agent or manager" or "professional and large business owner"). Forty-five percent of the children were firstborn and 53% were in day care. There were no significant differences between the proband or control groups for any of these factors.

Measures and Procedures

To provide optimal freedom from bias, maternal diagnostic, infant temperament, infant sleep, attachment, and parenting procedures were each coded independently by individuals blind to the other information.

Maternal Diagnoses and Symptoms

Mothers were interviewed using the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I/NP, Version 2.0 and SCID-II) (First et al., 1996). All interviews were videotaped and interrater reliability conducted on 20% of the sample showed no disagreements (Cohen κ = 1.00).

Infant Temperament

Four-Month High Reactivity. Temperament was measured for the 4-month cohort in the home using the procedures developed by Kagan and colleagues (Kagan, 1994). Infants sat in a reclining cushioned seat and heard some taped sentences, saw three different colorful mobiles move back and forth, had a cotton swab dipped in dilute butyl alcohol placed under the nostrils, heard a female voice speaking different syllables, and heard a balloon popped. During these procedures the mother was out of view of the infant. Videotapes were coded for high motor activity (multiple arm, leg, and back movements) and high crying (high percentage of time spent crying) in response to the stimuli. Infants were classified as high reactive (high motor activity and crying), low reactive (low motor activity and crying) or neither (either high motor activity and low crying or the opposite). Jerome Kagan, who had established interrater reliabilities with an independent judge ranging from 0.82 to 0.90 (Kagan et al., 1998), scored the videotapes. Three infants were not included because of taping problems.

Fourteen-Month BI. Temperament was measured for the 14-month cohort in the laboratory using the procedures developed by Kagan and colleagues (Kagan, 1994). These procedures involved the presentation of inanimate stimuli and interactions with strangers. The inanimate stimuli presented to the child included electrodes, a blood pressure cuff, a spinning bingo wheel with noisy objects inside, rotating toys, a puppet show, and sweet and sour tastes. In terms of interactions with strangers, several strangers in costumes attempted to interact with the child. These included a woman stranger (not the examiner), a woman dressed in a white laboratory coat and gas mask, and a woman with a black cloth over her head and shoulders. A child was classified as BI overall if he/she showed fear to four or more of the situations (equivalent to splitting the sample at the mean and median). Jerome Kagan, who had established high interrater reliabilities for fears (r = 0.89) (Kagan et al., 1998), scored the videotapes. Three infants were not included because of taping problems.

Parental Ratings of Infant Temperament. Mothers and fathers also completed the Infant Behavior Questionnaire (M.K. Rothbart, Infant Behavior Questionnaire, unpublished, 1978; Rothbart, 1981) for both cohorts. The Distress and Latency to Approach Sudden or Novel Stimuli subscale was used because this subscale was most likely to relate to high reactivity and BI. Some of the questionnaires were not completed and some were destroyed by water leakage, leaving questionnaires for 86% of the sample. There were no differences between the proband and control groups for the missing data. To decrease measurement error, maternal and paternal reports were averaged.

Infant Neurophysiology

Infant Salivary Cortisol. Cortisol was collected by having the child suck on a 6-inch-long cotton dental roll dipped in a few grains (0.025 g) of sugar-sweetened Kool-Aid™ drink mix to stimulate saliva flow and encourage compliance. Because of the possibility of assay interference with Kool-Aid™, measured amounts of stimulant were used in accordance with procedures that have been found to be accurate in prior research (Schwartz et al., 1998). When adequate saliva was absorbed by the dental roll, saliva was expressed into a vial using a needleless syringe and stored at –20°C. Home samples were refrigerated, mailed, and then stored at –20°C until assayed. Clements and Parker (1998) showed that general mailing should not affect cortisol values.

Because of the diurnal rhythm in HPA activity, the timing of the procedures and sampling were carefully controlled. Since the diurnal

rhythm might not be fully established for 4-month-old infants, the first cortisol sample was taken 20 minutes after the child had awakened from the morning nap, on average at 10:24 A.M. (SD = 58 minutes). For the 14- and 15-month procedures, the samples were taken at the same time of day for each child, with the first sample on average at 10:17 A.M. (SD = 12 minutes) and 10:32 A.M. (SD = 26 minutes), respectively.

For the 4-month cohort, infant salivary cortisol was collected in the home before and after the high reactivity temperament procedure and at the end of the visit, 20 minutes after mother–infant feeding, play, and still-face procedures. A fourth sample was collected in the home at the same time the following day by the mother, on average at 11:27 A.M. (SD = 61 minutes).

For the 14-month cohort, infant salivary cortisol was collected in the laboratory before, 20 minutes after the beginning, and at the end of the BI temperament procedure. Mothers were also instructed to take a home sample the following day at the same time, which was done on average at 11:47 A.M. (SD = 52 minutes).

The 15-month procedure included (1) initial collection of salivary cortisol; (2) SSP (described below); (3) parent–child interactions with free-play, clean-up, and structured tasks; (4) collection of salivary cortisol 20 minutes after the end of the SSP (or 40 minutes after the start of the visit); and (5) final collection of salivary cortisol at end of procedures. Mothers were also instructed to take a home sample the following day at the same time, which was done on average at 11:34 A.M. (SD = 43 minutes).

Cortisol assays were performed in duplicates on 50–100 μL of saliva, using a modification of the Corning CIBA Magic cortisol radioimmunoassay kit (Kirschbaum et al., 1989) with reagents manufactured by Chiron. Duplicate values differing by 20% or more were reassayed, and samples were excluded if insufficient saliva was available to reassay. Inter- and intra-assay coefficients of variation that were calculated using samples of known cortisol levels were 13% and 6%, respectively.

Lack of subject cooperation, insufficient saliva, contamination, infant illness, and laboratory error resulted in missing samples at each time point. Missing data included the following: 4-month high reactivity procedure (10–18%); 14-month BI procedure (24–36%); 15-month SSP procedure (28–42%). There were no significant associations between maternal diagnosis and the cortisol data being missing.

Infant Sleep. Sleep was assessed using parental questionnaires, daily logs, and videotaping separately for the 4- and 14-month cohorts. Mothers completed the questionnaires for the 4-month cohort when infants were an average of 5.5 months of age (SD = 2.0) and for the 14-month cohort when infants were an average of 15.4 months of age (SD = 1.4). Questionnaires included the Sleep Habits Questionnaire, a 64-item questionnaire that has demonstrated validity (Seifer et al., 1996). A subscale that assesses trouble settling at bedtime was used to measure infant sleep difficulties (e.g., child falls asleep within 20 minutes after going to bed, child is ready to go to bed at bedtime, child resists or struggles at bedtime). Mothers also reported the primary location for the infant's sleep (e.g., room with parent, bed with parent).

Sleep logs were completed by the mothers for the 4-month cohort at an average of 7.9 months of age (SD = 1.5) and for the 14-month cohort at an average of 15.9 months of age (SD = 1.5). The sleep log was completed for 14 consecutive days during a time when the child was not ill or experiencing changes (e.g., traveling or life stresses). The sleep log provided information including the number of nighttime awakenings, methods parents used to put the child to sleep (e.g., for each time the parent put the child to sleep, whether feeding or putting into bed awake was used), and the amount of time the child spent in his/her own bed (in hours and minutes). Child sleep disorders were classified using the sleep logs according to criteria described by Anders and colleagues (Gaylor et al., 2001), including five or more nights per week of two or more awakenings per night for infants between 1 and 2 years of age. Some of the questionnaires and sleep logs were not completed and some were destroyed by water leakage, leaving information for 68% to 82% of the sample. There were no significant differences between the proband and control groups for the data being missing.

For the 4-month cohort, sleep videotaping was conducted at an average of 8.0 months of age (SD = 1.4). This procedure was considered to be a pilot aspect of the research and was performed on the basis of personnel availability. Therefore, data were collected only for a total of 30 subjects (15 probands, 15 controls). Sleep-wake behavior was recorded with a portable time-lapse video system consisting of a time-lapse videocassette recorder and a low-level illumination camera. Video and audio signals were recorded using the 12-hour time-lapse mode so that a full 12 hours could be recorded on one standard VHS videotape, although real clock time was recorded on the tape. Videotapes were scored using a system developed by Anders and colleagues (Anders and Sostek, 1976; Gaylor et al., 2001) for number of awakenings lasting two or more minutes that occurred at least 10 minutes after initial sleep, percentage of time awake, and parental feeding during the night. Two research assistants achieved high interrater reliabilities with Anders (Anders and Sostek, 1976; Gaylor et al., 2001) (r = 0.80 to 1.00) and with each other (r = 0.82 to 0.95) on 25% of the sample for the sleep variables. Two consecutive nights of sleep were recorded in the infant's home, and the mean of these two nights was used.

Parenting Behaviors

Parenting Behaviors Toward Infants in the 4-Month Cohort When the Infants Were 4 and 8 Months of Age. Parenting behaviors were measured for the 4-month cohort at 4 and 8 months of age to obtain more complete information than could be obtained at only one age. Mothers and infants were videotaped for a total of approximately 6 hours in the home, first after the temperament procedure at 4 months of age and then at approximately 8 months of age (mean = 7.8, SD = 1.5) during normal daily routines (free and structured play, feedings, diaper change and bath). Videotapes were coded for sensitivity/insensitivity and cooperation/intrusiveness using scales developed by Ainsworth and colleagues (1978). In this scoring system, low scores for sensitivity and cooperation reflected ignoring or misreading the baby's signals and interrupting or limiting the child's activities. In addition, research assistants used a Q sort procedure (D.R. Pederson, G. Moran, S. Bento, Maternal Behavior Q sort Manual, Version 3.1, unpublished, 1994; Pederson and Moran, 1995) to score maternal sensitivity. As is standard with Q sort variables, the Fisher transformation was applied to the Q sort variable to normalize the distribution (Cohen and Cohen, 1975). Since the two scales developed by Ainsworth (sensitivity/insensitivity and cooperation/interference) and the Q sort scores were all highly correlated (r = 0.82 to 0.94, $p < .01$), a mean of the standardized scores was used for the analyses. Interrater reliability conducted on the composite score for 20% of the sample was high (r = 0.98). Two infants were not included because of taping problems.

Parenting Behaviors for 14-Month Cohort at 15 Months of Age. Mothers completed the Parenting Scale (Arnold et al., 1993) when the children were approximately 15 months of age (SD = 2.5) to examine parenting behaviors in disciplinary situations. This questionnaire provided an overall index of less effective parenting in disciplinary situations, as well as three subscales: Laxness (inconsistent limit-setting), Overreactivity (showing anger in response to child behaviors such as arguing, yelling, or insulting), and Verbosity (talking a lot with the child about disciplinary situations) (Arnold et al., 1993). The total score and subscales have demonstrated good internal consistency, test-retest reliability over

a 2-week period, and validity, significantly distinguishing between a nonclinical and clinical sample with behavior problems (Arnold et al., 1993). In addition, the total score and subscale scores reported by mothers have been significantly associated with the same behaviors observed and rated by research assistants (Arnold et al., 1993).

Infant–Parent Relationships

Strange Situation Procedure. Mothers and infants participated in the SSP (Ainsworth et al., 1978), which consisted of eight episodes, including two brief separations from and reunions with the mother. Attachment group classification was assigned using the traditional ABC criteria, based primarily on the infant's reactions to the mother's return (Ainsworth et al., 1978). Infants who actively greeted and/or sought contact with the mother upon reunion and returned to exploration within 3 minutes were classified as secure (group B). Infants who actively averted gaze or avoided or ignored the mother immediately upon reunion were classified as avoidant (group A). Infants who sought to reunite with the mother but displayed ineffective proximity and contact-seeking behavior, showing anger and active resistance to contact or prolonged fussiness and persistent low-level distress, were classified as ambivalent/resistant (group C). Videotapes were also scored separately for disorganization (D classification) (Main and Solomon, 1990). Infants who showed unusual behaviors such as fear of the mother, freezing, hitting, or running from the mother were classified as disorganized (group D). Videotapes were scored by the researchers who coded the large federally funded National Institute of Child Health and Human Development Study of Early Child Care, using the standard classification systems (Ainsworth et al., 1978; Main and Solomon, 1990). Interrater reliability was conducted on 20% of the sample ($\kappa = 0.81$ for ABC classification; $\kappa = 0.67$ for D classification). Final scores for difficult tapes and coder disagreements were based on consensus.

Data Analyses

All of the main hypotheses centered on differences between the group with maternal PD and the control group. Thus χ^2 tests were used for the categorical variables, and *t* tests (if data were normally distributed) or Mann-Whitney *U* tests were used for the continuous variables. Because the cortisol data were not normally distributed, even with logarithmic transformations, ranked scores were used for repeated-measures analyses of variance (ANOVAs) examining repeated cortisol samples that were taken in the same location (home or laboratory). Two-tailed tests were used in all cases. Analyses using Pearson correlations were conducted to examine the interrelations among infant sleep and parenting behaviors with regard to infant sleep. Point biserial correlations were used for correlations between continuous and binary variables.

RESULTS

Maternal Diagnoses and Symptoms

Additional diagnoses for mothers with PD included agoraphobia (64%), social phobia (64%), generalized anxiety disorder (44%), specific phobia (64%), posttraumatic stress disorder (40%), lifetime major depression (71%), other depressive disorder (13%), depressive disorder during the child's life (47%), alcohol abuse/dependence prior to the pregnancy (49%), non–alcohol abuse/dependence prior to the pregnancy (31%), anorexia nervosa (11%), and bulimia nervosa (4%). Mothers with PD averaged a total of eight limited-symptom and full panic attacks per month (SD = 10.6) and had experienced symptoms for almost one third of the child's life; 19% were in treatment. Twenty-two percent of the control parents reported a history of alcohol abuse/dependence (usually drinking at college parties) but no use of alcohol since becoming pregnant with the child.

Maternal PD and Infant 4-Month Temperament

Infants of mothers with PD were not significantly more likely than controls to show high versus low reactivity ($\chi^2 = 2.68$, $p = .10$). In fact, infants of mothers with PD showed somewhat higher rates of low reactivity (61% of the total sample) than controls (35% of total sample) (Table 1). Further investigations of the dimensions used

TABLE 1
Infant Temperament by Maternal Diagnostic Group

Infant Temperament	Maternal Panic Disorder	Maternal Controls
Four-month cohort at 4 months of age		
Reactivity[a]		
High reactivity (%)	5 (22)	9 (39)
Low reactivity (%)	14 (61)	8 (35)
Neither high nor low reactivity (%)	4 (17)	6 (26)
High motor (%)[a]*	6 (26)	14 (61)
High cry (%)[a]	8 (35)	10 (43)
Distress & Latency to Approach Stimuli: mean (SD)[b]**	2.75 (0.84)	2.07 (0.56)
Fourteen-month cohort at 14 months of age		
Behaviorally inhibited (%)[b]	11 (46)	7 (39)
Distress & Latency to Approach Stimuli: mean (SD)[c]	2.77 (0.63)	3.16 (0.60)

[a] $n = 46$.
[b] $n = 42$.
[c] $n = 30$.
* $p < .05$; ** $p < .01$.

TABLE 2
Infant Salivary Cortisol Means (and Standard Deviations) by Maternal Diagnostic Group and Study Condition

	Maternal Panic Disorder	Maternal Controls
Home salivary cortisol sampling at 4 months (4-month cohort) (n = 36)[a]*		
Start of visit	0.78 (1.41)	0.39 (0.32)
After high reactivity procedure	0.68 (1.27)	0.35 (0.31)
End of visit	0.43 (0.45)	0.30 (0.15)
Twenty-four hours later	0.54 (0.63)	0.36 (0.32)
Laboratory salivary cortisol sampling at 14 months (14-month cohort) (n = 27)[a]*		
Start of procedures	0.28 (0.15)	0.13 (0.12)
Twenty minutes later	0.47 (0.32)	0.27 (0.19)
End of procedures	0.36 (0.19)	0.29 (0.14)
Home salivary cortisol sampling at 14 months (14-month cohort) (n = 31)[b]	0.35 (0.17)	0.43 (0.33)
Laboratory salivary cortisol sampling at 15 months (14-month cohort and subsample of 4-month cohort) (n = 44)[a]*		
Start of procedures	0.30 (0.26)	0.20 (0.11)
Forty minutes later	0.34 (0.32)	0.15 (0.09)
End of procedures	0.24 (0.15)	0.23 (0.32)
Home salivary cortisol sampling at 15 months (n = 41)[b]	0.28 (0.15)	0.27 (0.17)

[a] Repeated-measures analysis of variance: * diagnosis significant at $p < .05$; time not significant (NS); interaction NS.
[b] Mann-Whitney U test: diagnosis NS.

to score observed high reactivity revealed that motor activity could have accounted for the high reactivity findings, with infants of PD mothers displaying significantly less motor activity than controls ($\chi^2 = 5.66$, $p < .02$). In contrast, PD parents rated their infants as more likely to show Distress and Latency to Approach Sudden or Novel Stimuli ($t = 2.32$, $p < .03$).

Maternal PD and Infant 14-Month Temperament

There were no significant findings for overall infant BI classification by maternal diagnostic group. Parental ratings of infant temperament revealed a trend for lower Distress and Latency to Approach Sudden or Novel Stimuli ($t = –1.72$, $p < .10$) in infants with PD mothers compared to controls.

Maternal PD and Infant Salivary Cortisol

Means, standard deviations, and the results for the main hypotheses concerning infant salivary cortisol are presented in Table 2. All three of the repeated-measures ANOVAs showed significant main effects for maternal diagnosis, but not for time or the interaction between time and diagnosis. In other words, as predicted, infants of mothers with PD in both cohorts showed significantly higher salivary cortisol levels than infants of mothers without psychopathology at 4 months of age and in the laboratory procedures at 14 and 15 months of age. In contrast to salivary cortisol levels measured in the laboratory, the home salivary cortisol levels for the 14- and 15-month-old children were not significantly different for the infants with PD mothers compared to controls.

Infant Sleep Variables

Trouble settling to sleep was significantly associated with greater number of infant awakenings for both the 4- ($r = 0.63$, $p < .01$) and 14-month ($r = 0.46$, $p < .05$) cohorts. For the 4-month cohort at 5 to 8 months of age, correlations among the videotaped variables and between the videotaped and parent-reported variables were generally low to moderate ($r = –0.21$ to 0.31). The only exception was that number of awakenings was significantly and highly correlated with percentage of time awake ($r = 0.64$, $p < .01$).

Infant Sleep and Parenting Behaviors With Regard to Infant Sleep

Intercorrelations among the infant sleep variables and parenting behaviors with regard to infant sleep showed some moderate to high relations. Parents who tended to feed their children to put them to sleep and tended not to put them into bed awake reported more infant trouble settling to sleep (4 month: feeding $r = 0.46$, $p < .01$, put down awake $r = –0.34$, not significant; 14 month: feeding $r = 0.38$, not significant, put down awake $r = –0.44$, $p < .05$) and more infant awakenings (4 month: feeding $r = 0.53$, $p < .01$, put down awake $r = –0.37$, $p <$

TABLE 3
Infant Sleep Characteristics and Parenting Behaviors With Regard to Infant Sleep Means (and Standard Deviations)

	4-Month Cohort at 5–8 Months of Age		14-Month Cohort at 15–16 Months of Age	
	Maternal Panic Disorder	Maternal Controls	Maternal Panic Disorder	Maternal Controls
Sleep characteristics				
Trouble settling (SHQ)[a]	1.53 (0.32)	1.50 (0.25)	1.59 (0.45)	1.32 (0.24)*
No. of awakenings (LOG)[b]	1.46 (0.98)	1.31 (0.83)	1.41 (1.08)	0.55 (0.60)*
No. of awakenings (CODE)[c]	3.80 (1.51)	2.63 (1.24)*	NA	NA
% time awake (CODE)[c]	0.15 (0.07)	0.09 (0.06)*	NA	NA
Parenting behaviors with regard to infant sleep				
% time feeding used for sleep (LOG)[b]	81 (33)	68 (38)	66 (45)	14 (32)**
% time feeding during night (CODE)[c]	6.67 (11.25)	1.11 (4.30)	NA	NA
% time put down awake (LOG)[b]	31 (34)	46 (38)	39 (42)	79 (35)*
Share room with parent (SQ) (%)[d]	4 (21)	4 (19)	8 (44)	0 (0)*
Share bed with parent (SQ) (%)[d]	4 (21)	3 (14)	6 (33)	0 (0)*
Hours in own bed (LOG)[e]	7.79 (4.01)	9.07 (1.99)	6.87 (3.91)	10.42 (1.06)*

Note: NA = no data are in these cells because sleep coding from videotapes was done only for a subsample of the 4-month cohort and not for the 14-month cohort; SHQ = Sleep Habits Questionnaire; LOG = sleep log; CODE = sleep coding from videotapes; SQ = sleep questions about primary sleep location.

[a] 4-month cohort: $n = 41$; 14-month cohort: $n = 30$.
[b] 4-month cohort: $n = 35$; 14-month cohort: $n = 24$.
[c] 4-month cohort: $n = 30$.
[d] 4-month cohort: $n = 40$; 14-month cohort: $n = 31$.
[e] 4-month cohort: $n = 33$; 14-month cohort: $n = 19$.
* $p < .05$; ** $p < .01$.

.05; 14 month: feeding $r = 0.58$, $p < .01$, put down awake $r = -0.49$, $p < .05$). Moreover, for both cohorts, infants who spent less time in their own beds and who did not sleep separately from their parents were significantly more likely to show disturbed sleep (4 month: $r = 0.40$ to 0.70, $p < .05$; 14 month: $r = 0.60$ to 0.78, $p < .01$).

Maternal PD, Infant Sleep, and Parenting Behaviors With Regard to Infant Sleep

Means, standard deviations, and the results for the main hypotheses concerning infant sleep are presented in Table 3. Infants from the 4-month cohort with PD mothers were significantly more likely to show more awakenings and a greater percentage of time awake during the night on the videotapes at 8 months of age than controls. Similarly, infants from the 14-month cohort with PD mothers were significantly more likely to have trouble settling and more awakenings than controls, as measured with the sleep logs.

Six of the infants older than 12 months of age met criteria for a sleep disorder. All of these infants were infants of mothers with PD. Significantly more infants of mothers with PD (43%) were classified as having a sleep disorder than controls (0%) (Fisher exact test $p = .02$).

In terms of parenting behaviors with regard to infant sleep, there was a trend for PD parents with 8-month-old infants (from the 4-month cohort) to be observed feeding their infants more during the night than controls ($t = 1.79$, $p = .09$). PD mothers of infants from the 14-month cohort reported putting their children to sleep with feedings a significantly greater percentage of the time and putting the child to bed awake a significantly smaller percentage of the time than controls. PD mothers of infants from the 14-month cohort also reported sharing a room or bed with their child at significantly higher rates than controls. In addition, children of PD mothers from the 14-month cohort spent significantly less time in their own beds than infants of parents without psychopathology.

Because breast-feeding infants have been thought to sleep differently than non–breast-feeding infants (more arousals and more feedings at night) (Thomas, 2000), rates of breast-feeding were examined and were found not to be significantly different for the proband and control groups. Eighty-two percent of mothers with PD breast-fed their children compared with 85% of the controls ($p = .78$).

Because both maternal diagnosis and parenting behaviors with regard to infant sleep were significantly associated with infant sleep, and because maternal diagnosis

TABLE 4
Parenting Behaviors and Infant–Parent Relationship by Maternal Diagnostic Group

	Maternal Panic Disorder	Maternal Controls
Parenting behaviors		
Four-month cohort at 4 and 8 months of age		
Maternal sensitivity: mean (SD)[a]**	–0.33 (0.96)	0.24 (0.96)
Fourteen-month cohort at 15 months of age		
Total less effective parenting in disciplinary situations: mean (SD)[b]*	2.56 (0.42)	2.25 (0.53)
Laxness: mean (SD)	2.36 (0.52)	2.12 (0.80)
Overreactivity (anger): mean (SD)**	2.35 (0.61)	1.77 (0.49)
Verbosity: mean (SD)	2.97 (0.68)	2.84 (0.77)
Infant–parent relationship		
Fourteen-month cohort and subsample of 4-month cohort at 15 months of age		
Attachment classification (ABC only)[c]		
Group A (avoidant attachment) (%)	7 (20)	7 (19)
Group B (secure attachment) (%)	21 (60)	21 (58)
Group C (ambivalent/resistant attachment) (%)	8 (22)	7 (20)
D Attachment classification (disorganized) (%)[c]	4 (11)	6 (17)

[a] $n = 47$.
[b] $n = 46$.
[c] $n = 71$.
* $p < .05$; ** $p < .01$.

was significantly associated with parenting behaviors with regard to infant sleep, a post hoc analysis examined whether parenting behaviors with regard to infant sleep could perhaps be partially responsible for the effects of maternal diagnosis on infant sleep. To explore this possibility, partial correlations were conducted to examine the relations between maternal diagnosis and infant sleep, after controlling for parenting behaviors with regard to infant sleep. All of these partial correlations were nonsignificant (r = 0.08 to 0.28). The findings were thus consistent with the premise that parenting behaviors with regard to infant sleep might be responsible for the sleep differences between infants of PD mothers and controls.

Maternal PD and Parenting Behaviors for 4- to 8-Month-Old Infants (Sensitivity)

PD mothers showed significantly lower levels of sensitivity toward their infants ($t = 2.04$, $p < .05$) (Table 4).

Maternal PD and Parenting Behaviors for 15-Month-Old Infants (Disciplinary)

PD mothers were significantly more likely to report less effective disciplinary parenting behaviors ($t = 2.15$, $p < .04$). Examination of differing aspects of this less effective parenting behavior revealed that PD mothers were significantly more likely to describe themselves as displaying anger toward their children in disciplinary situations ($t = 3.55$, $p < .01$).

Maternal PD and Infant–Parent Relationships

No significant differences were found between the maternal diagnostic groups for ABC attachment classification and D classification (Table 4).

DISCUSSION

Clear behavioral differences for infants with PD mothers were not seen in this research, but divergences concerning infant neurophysiology and parenting behaviors were identified. Infants with PD mothers had higher levels of salivary cortisol than controls at 4 months of age and in procedures at 14 and 15 months of age. Infants with PD mothers were also identified as showing more disturbed sleep than controls at 8 months of age and at 15 to 16 months of age. In addition, significant differences were seen between PD mothers and controls in terms of several types of parenting behaviors. PD mothers displayed parenting behaviors that could be associated with disturbed infant sleep (more maternal feedings at night, not putting the children to bed awake, and sleeping with the children) and were observed to be less sensitive with their 4- to 8-month-old infants than controls. PD mothers also reported less effective parenting behaviors in disciplinary situations with their 15-month-old toddlers than mothers without psychopathology, describing more displays of anger toward the children.

This research suggested that young infants with PD mothers could be experiencing higher levels of arousal/arousability but might not display such reactions behaviorally. One possible explanation for this lack of display could be prenatal stress. Research has suggested that more stressful pregnancies contribute to lower motor activity in the infants (Schneider and Coe, 1993). Studies with depressed mothers have similarly described decreased infant motor tone and reactivity to inanimate stimuli (Field, 1995). In the present study, infants with PD mothers were significantly less likely to show high motor activity than controls. Perhaps PD mothers had experienced panic attacks and more stress during pregnancy, which could have contributed to lower infant motor activity, which could have played a role in decreased classification of proband infants as highly reactive.

In contrast to the observational ratings, PD parents rated their 4-month-old infants as significantly more distressed in response to stimuli than controls. The parents could have been seeing and responding to slightly different behaviors; the questionnaire characterized reactivity in response to more typical daily situations (e.g., washing, feeding, animals) than to novel stimuli. However, the reports supported the hypothesis of increased arousal/arousability in infants with PD mothers.

In contrast to the unclear and inconsistent findings in terms of behavioral reactivity in the young children, this research demonstrated somewhat more clear findings with regard to greater neurophysiological arousal/arousability in infants with PD mothers compared to controls, as measured with salivary cortisol and sleep. Previous research has shown important relations between elevated salivary cortisol levels and risk status (Goldsmith and Lemery, 2000; Granger et al., 1994, 1998; Schmidt et al., 1997). In the current study, salivary cortisol levels were significantly higher for both the younger and older infants with PD mothers compared to controls. Because these same infants with PD mothers did not show more highly reactive or behaviorally inhibited temperament compared to controls, neurophysiological indicators, such as salivary cortisol, might be one of the few methods available for identifying young infants at risk.

Similarly, disturbed sleep might be an early indicator of risk for psychopathology. Seifer and colleagues (1996) found that more disturbed sleep in young children was associated with the presence of psychiatric illness in the parents (in a sample of parents with major depression, anxiety disorders, or no psychopathology) and was significantly associated with child symptoms of psychopathology. Yamada and Dawson (1997) similarly found children of depressed parents to have more disturbed sleep. Multiple studies have also connected disturbed sleep with psychopathology (Benca, 1996; Johnson et al., 2000; Kazarian et al., 1978).

In an effort to clarify potential reasons for associations between psychopathology and disturbed sleep, Seifer and colleagues (1996) outlined several possible mechanisms: (1) sleep variation might be a causative factor in the development of clinical disturbance, (2) sleep disturbance might be part of the clinical syndrome that defines a mental disorder, (3) sleep characteristics might be markers for mental disorders but not have a functional role in the etiology of the disorder, and (4) sleep changes might emerge after the onset of mental illness. The fourth possibility would appear less likely based on the fact that several studies, including the present investigation, have shown infants of parents with psychopathology to have sleep disturbances (Seifer et al., 1996; Yamada and Dawson, 1997). Sleep disturbances in infants at risk have thus been found to precede psychopathology, suggesting that these sleep disturbances might not simply be the result of mental illness but might portend or contribute to psychopathology. In addition, infants of parents with psychopathology could have disturbed sleep because such parents might have difficulties signaling safety, might tend to contribute to increased arousal, and/or might have less knowledge or skills for settling infants to sleep.

The current research appeared to support the latter hypotheses concerning parenting behaviors, because parenting behaviors were found to influence infant sleep and were perhaps responsible for the associations between maternal PD and disturbed infant sleep. Maternal PD was found in this study to be associated with higher rates of feeding the infant at bedtime, lower rates of putting the infant to bed awake, and more time sleeping with the infant. These factors were also significantly correlated with disturbed infant sleep in the current analyses. Previous research has shown that feeding children at bedtime has been associated with more disturbed sleep (Wolfson et al., 1992). Putting infants to bed awake and having them sleep separately from their parents has been found to facilitate infant sleep (Wolfson et al., 1992). Infants with parents who have psychopathology might have more disturbed sleep because the parents have engaged in behaviors that do not facilitate infant sleep. Alternatively, parents might engage in these behaviors because the infants initially

showed more sleep difficulties. The current research could not resolve these issues but suggested that disturbed sleep in infants of PD mothers compared to controls could be mediated by parenting behaviors.

Differences in parenting behaviors for PD mothers and controls were also observed for daytime activities and disciplinary situations. PD mothers were less sensitive in play and daily activities (bath, dressing) and reported displaying more anger in disciplinary situations. PD mothers could have shown less sensitive parenting behaviors in this study because of their own childhood experiences (Rapee, 1997). PD mothers might also have trouble responding to infant signals because of preoccupation with anxiety. At home with their infants, some PD mothers appeared distracted and less attentive to infant emotions and signals. The mothers might have been focused instead on feelings of anxiety. In addition, PD mothers might not only have difficulties managing feelings of anxiety but perhaps also anger. PD mothers might have reported displaying more anger in disciplinary situations because of such emotional regulation difficulties.

Previous research has suggested that less parental sensitivity might contribute to later anxiety disorders by influencing the infant–parent attachment relationship. Children who have experienced less parental sensitivity early in life are at greater risk for developing insecure attachment relationships (Ainsworth et al., 1978), and toddlers with insecure attachment relationships are at higher risk for developing anxiety disorders later in childhood and adolescence (Warren et al., 1997). Angry emotional displays could contribute to anxiety disorders through similar mechanisms. Less parental sensitivity and more parental anger could thus promote anxiety disorders by undermining the child's sense of security and competence. Moreover, such parenting behaviors have been associated with child problems (Arnold et al., 1993). However, this research did not find attachment relationship differences between the diagnostic groups. Thus the impact of the differences in parenting behaviors and mechanisms of influence are not entirely clear at this very early phase of development.

Some researchers have suggested that the combination of increased child arousal/arousability and parenting behaviors might be most influential in terms of predicting later anxiety disorders (Manassis and Bradley, 1994). Infants with more neurophysiological arousal/arousability could be more sensitive—than children with less—to parenting behaviors that contribute to psychopathology. In other words, certain types of parenting behaviors could contribute to anxiety disorders particularly for more aroused/arousable children. Further research using longitudinal approaches is needed to clarify the impact of parenting behaviors on children with increased neurophysiological arousal/arousability. Helping PD mothers parent their neurophysiologically aroused/arousable children could reduce risk for psychopathology.

Limitations and Directions for Future Research

This research was limited by small sample sizes; thus an absence of findings could not be interpreted as indicative of negative results. With a larger sample, it also would have been interesting to examine in more detail differences based on different types of psychopathology. For example, differences between several different comparison groups (e.g., PD mothers with and without major depression) could have been examined, as has been done in previous research (Rosenbaum et al., 2000), in order to more fully delineate possible differing contributions of specific types of maternal psychopathology. Exploratory analyses did not reveal evidence for any other type of psychopathology (e.g., depression) accounting for the findings. However, since there were not large enough separate groups of mothers with different types of psychopathology (without PD), it was not possible to completely test such hypotheses. Another limitation was that diagnostic interviews were not conducted with the fathers in this pilot work. Psychopathology in the fathers could also contribute to differences in infant behaviors and neurophysiology.

In addition, the subjects were generally white and middle- to upper-middle-class. Thus the results might not be applicable to the general population. There could also have been differences between the current sample and the previous samples in which associations were found between maternal PD and infant BI (Rosenbaum et al., 1988, 2000). Rosenbaum and colleagues used clinic- and hospital-based recruitment, in contrast to the community-based procedures used for this research. The PD parents in previous research might thus have exhibited more severe disorders, which could have accounted for the different findings. Rosenbaum and colleagues (1988, 2000) also examined older children. Behavioral differences might not be apparent at such young ages or might only be evident at younger ages in very specific contexts (such as sleep).

An additional limitation was that the research was cross-sectional. This design did not allow for the investigation of changes over time or the exploration of whether

parenting behaviors influenced the infant over time or whether the infant influenced parenting over time. Longitudinal research is needed to investigate whether the 4- and 14-month-old infants with PD parents actually do become BI at older ages, perhaps as a result of parenting experiences. Future research should also use a longitudinal design to clarify issues of directionality, particularly in relation to investigating the impact of parenting behaviors on infant sleep. Longitudinal research with high-risk infants could potentially also provide information to distinguish between different mechanisms linking psychopathology and sleep disturbances (e.g., whether sleep disturbances could contribute to psychopathology or merely provide information concerning risk).

Clinical Implications

If these research findings were replicated and extended, higher levels of salivary cortisol and disturbed sleep in infancy could be used to identify children at risk for developing psychopathology. Because both salivary cortisol and sleep disturbances are easily measured, children could be routinely screened during pediatric visits and referred for appropriate interventions.

Almost half (43%) of the infants with PD mothers met criteria for a sleep disorder. Thus infants with PD mothers not only had more disturbed sleep generally than controls, but they also had higher rates of sleep disorders. It might thus be important to evaluate infants with PD mothers for sleep disorders. Such families could likely benefit from treatment and/or preventive interventions. Since previous research has found disturbed sleep in infants of depressed and generally anxious parents (Seifer et al., 1996; Yamada and Dawson, 1997), it might be useful to screen these families in addition.

This study also supported previous research describing parenting behaviors that facilitate infant sleep. Feeding frequently at bedtime was associated with more disturbed sleep, and putting infants to bed awake (in a separate room) was associated with better sleep. Clinicians could instruct and support parents in the use of appropriate strategies that are likely to facilitate infant sleep. Providing this information to families with psychopathology might be particularly beneficial in light of the increased risk for sleep disorders.

This study, along with previous research (Manassis et al., 1994; Weinberg and Tronick, 1998; Whaley et al., 1999), also emphasized the importance of evaluating parenting behaviors in mothers with anxiety disorders. The particular aspects of parenting that this study highlighted (in addition to behaviors concerning infant sleep) included parental sensitivity and displays of anger in disciplinary situations. Because anxious mothers have insecure attachment relationships themselves (Manassis et al., 1994), they might have difficulties in their relationships with others. It would thus be essential that the mother not feel criticized but rather feel supported by the therapist in her interactions with her child. In other words, it would be important for the therapist to provide a "secure base" for the mother so that she could provide such a "secure base" for the child (Bowlby, 1997). The approach to treatment might initially include some discussion concerning how the mother experiences and views the child, so the therapist could gain insight into the mother's perspective. Knowing the mother's perspective, the clinician could then focus the mother on the baby's needs and on how the mother's behavior with the child could promote the child's development. For example, clinicians could conduct sessions with the mother and baby, asking the mother to describe what she thinks her infant needs and helping her learn to accurately read the child's cues, thus facilitating increased maternal sensitivity. In addition, the therapist could help the mother manage anger she might feel toward her child. By discussing such emotions, mothers might recognize their feelings more readily and learn to control their responses toward their children in disciplinary situations. Not only could clinicians utilize such interventions, but the effectiveness of the interventions could be tested experimentally.

For clinicians, this research supported a focus on the evaluation of parenting behaviors and sleep for young infants. Clinicians who direct evaluative efforts, not just on child symptoms but also on parenting behaviors, could be making significant contributions to improved child outcomes. Furthermore, clinicians who identify and treat children with disturbed sleep might not only be alleviating current suffering, but also could be preventing future psychopathology.

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