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Coregulation in Salivary Cortisol During Maternal Holding of Premature Infants

Madalynn Neu, RN, PhD, Mark L. Laudenslager, PhD, and JoAnn Robinson, PhD

Purpose: The purpose of this study was to examine coregulation between mothers and preterm infants in hypothalamic-pituitary-adrenocortical (HPA) system activity, as indicated by salivary cortisol levels, while mothers held their infants. The research questions were (a) does mother–infant coregulation in HPA activity occur during holding? and (b) if mother–infant coregulation in HPA activity exists during holding, do type of holding, antenatal steroids, sound level, and maternal touch influence this coregulation? *Sample:* The sample consisted of 20 mother–infant dyads with infants at a mean postconceptional age of 34.7 weeks ($\pm$0.7) and average postnatal age of 15 days ($\pm$9) at the time of cortisol sampling. *Design:* The design was exploratory using convenience sampling. Maternal and infant cortisol levels were obtained at Time 1 (baseline) and Time 2 (end of holding); at each time, the absolute differences in levels between mother and infant were determined. Coregulation was operationalized as less difference between maternal-infant cortisol levels immediately after holding (Time 2) as compared to before holding (Time 1). *Results:* The two variables with the highest correlation with the Time 1/Time 2 difference score included antenatal steroids and ambient sound level, which were entered into a linear regression equation as predictor variables. A coregulatory relationship in cortisol levels existed between mothers and infants during holding, which was moderated by sound levels. Nurses in the neonatal intensive care unit (NICU) can facilitate the mother–infant relationship, as reflected in coregulatory measures, by promoting a quiet environment, particularly around mothers who are holding their infants.

Keywords: coregulation; mother–infant interaction; salivary cortisol; holding; NICU; preterm infant

Coregulation is defined by Fogel (1993) as a process in which "individuals dynamically alter their actions with respect to the ongoing and anticipated actions of their partners" (p. 34). In humans, maternal-infant coregulation during face-to-face interactions has been associated with the development of self-regulation. Researchers have begun to examine coregulation in physiologic processes between mother and infant, but to date few studies have been done. Holding is one of the first interactions that occur between mother and infant. For preterm infants hospitalized in neonatal intensive care units (NICUs), holding is an especially important facilitator for the maternal-infant relationship. Research on preterm infants primarily addresses kangaroo (skin-to-skin) holding, in which the mother holds the infant vertically in skin-to-skin contact. This research suggests that kangaroo holding has a positive effect on infant development and the mother–infant relationship (Feldman & Eidelman, 2003; Feldman, Weller, Sirota, & Eidelman, 2002; Ludington-Hoe et al., 1999).

Researchers have identified coregulatory interactive activities between mother and infant during traditional holding of young infants (Jonsson et al., 2001). These activities were described as a maternal vocal response of similar temporal duration and rhythm as an infant head droop or similar vocal emotional intensity as displayed in an infant's behavior. Little research, however, has been done on the physiologic interplay between mother and infant during holding. Salivary cortisol, an

From the School of Nursing (MN) and Department of Psychiatry (MLL), University of Colorado at Denver and Health Sciences Center, Denver, Colorado; and Department of Early Childhood Education, University of Connecticut, Connecticut (JAR).

Address correspondence to Madalynn Neu, UC Denver College of Nursing, Anschutz Medical Campus, College of Nursing, C288-19, Education 2 North Room 4322, 13120 E 19th Ave, Aurora CO 80045; phone: 303-724-8550; e-mail: Madalynn.neu@ucdenver.edu.

indicator of the activity of the hypothalamic-pituitary-adrenocortical (HPA) system (Kirshbaum & Hellhammer, 1989; Laudenslager, Bettinger, & Sackett, 2006), may serve as a responsive signal that permits measurement of synchronous physiological processes in the mother and infant.

The purpose of the current study was to examine coregulation between mothers and preterm infants in HPA activity, as indicated by salivary cortisol levels, while mothers held their infants. Our research questions were (a) does mother–infant coregulation in HPA activity, as indicated by salivary cortisol levels, occur during holding? and (b) if mother–infant coregulation in HPA activity occurs during holding, do type of holding, antenatal steroids, sound level, or maternal touch influence this coregulation? We hypothesized that (a) kangaroo holding will positively influence coregulation in HPA activity; (b) no use of antenatal steroids will positively influence coregulation in HPA activity; (c) low sound levels will positively influence coregulation in HPA activity; and (d) contingent maternal touch will positively influence coregulation in HPA activity.

Background

Mother–Infant Coregulation

The mother–infant behavioral coregulation that occurs during face-to-face interactions has been studied for several decades. Researchers have described this process as synchrony (Feldman, 2006; Karger, 1979), interpersonal contingency (Jaffe, Beebe, Feldstein, Crown, & Jasnow, 2001), coordination (Tronick & Cohn, 1989), mutual regulation (Lester, Hoffman, & Brazelton, 1985), and attunement (Jonsson et al., 2001; Stern, Hofer, Haft, & Dore, 1985). In a coregulatory interaction, activities of the two members of the dyad may occur sequentially or simultaneously and involve continuous adjustments on the part of both members. At least one member of the dyad contingently adapts his or her behavior to accommodate or modify the behavior of the other to achieve greater synchrony. Fogel and Garvey (2007) present the example of a mother tickling her infant. The mother initiates the activity, but the dyad's actions then flow continuously in relation to one another so that neither one can be identified as the leader (p. 253). Coregulation in the mother–infant interaction is an important contributor to the infant's cognitive and self-regulatory development (Feldman, Eidelman, & Rotenberg, 2004; Hui-Chin & Fogel, 2003; Jaffe et al., 2001) and to mother–child attachment patterns (Isabella & Belsky, 1991).

Physiologic coregulation between mother and infant has been studied far less than interactional coregulation and, when studied, has been measured as a correlation. One study (Bornstein & Suess, 2000) suggested a coregulatory interaction in vagal-tone responsiveness between mother and infant during infant completion of a visual habituation task. Mothers and their infants showed no correlation in vagal tone at baseline but demonstrated a slight correlation during the task ($r = .23$). Results suggest that when members of the dyad share an experience, physiologic functions of one member of the dyad may begin to resemble the physiologic functions of the other.

Salivary Cortisol

Salivary cortisol, a marker of HPA system activity, correlates highly with plasma cortisol, reflects the unbound cortisol in the body, is relatively easy to collect, and is a valid indicator of HPA system function (Aardel & Holm, 1995; Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Kirschbaum & Hellhammer, 1989; Laudenslager et al., 2006). Salivary cortisol measures have been validated against serum cortisol measures in preterm infants (Calixto, Martinez, Jorge, Moreira, & Martinelli, 1995). Although adults typically display a diurnal pattern of cortisol secretion (Kirschbaum & Hellhammer, 1989), most infants do not reliably display this pattern in the early months of life (de Weerth, Zijl, & Buitelaar, 2003; Neu, Goldstein, Gao, & Laudenslager, 2007).

In animal studies, plasma-free and total cortisol levels increased in nonhuman primate infants when they were separated from their mothers but returned to normal when they were reunited (Laudenslager et al., 1995). Rat pups of mothers who spent more time licking and grooming their pups during the first days of life displayed reduced corticosterone response to stress and better feedback sensitivity than offspring of mothers who groomed less (Liu et al., 1997; Meaney, Aitken, van Berkel, Bhatnagar, & Sapolsky, 1988). Individual maternal and infant cortisol levels show changes during holding (Morelius, Theordorsson, & Nelson, 2004), and these changes may be interactive.

Potential Influences on Mother–Infant Cortisol Coregulation During Holding

Many factors may influence the effect of holding on maternal-infant coregulation in HPA activity. In the present study, we looked specifically at type of

holding, maternal treatment with antenatal steroids, sound level in the nursery, and maternal touch.

Holding. Holding an infant may be an effective means by which to achieve physiologic coregulation between the infant and the caregiver. Most research conducted on holding focuses on the kangaroo (skin-to-skin) method in which the infant is held vertically in skin-to-skin contact on the chest of the mother or caregiver. The caregiver wraps her clothing around the infant, simulating a kangaroo pouch, to maintain the infant's temperature. Benefits of kangaroo holding for mothers are feelings of well-being, intense connectedness with the infant, and increased self-confidence in their ability to care for the infant (Affonso, Bosque, Wahlberg, & Brady, 1993; de Macedo, Cruvinel, Lukasova, & D'Antino, 2007; Feldman, Eidelman, Sirota, & Weller, 2002; Neu, 1999). Researchers have reported improved mother–infant interaction, including positive affect, sensitive and nonintrusive maternal touch, adaptation to infants cues, mother–infant mutual gaze, and successful breastfeeding, when dyads practiced kangaroo holding at least 1 hr a day during hospitalization of the preterm infant (Feldman & Eidelman, 2003; Feldman et al., 2002; Rojas et al, 2003). The positive findings regarding kangaroo care suggest that it promotes interactional coregulation. For example, Ludington-Hoe et al. (2006) reported thermal synchrony during kangaroo holding of twins. As twins were held simultaneously in skin-to-skin contact, each maternal breast temperature responded to the thermal needs of the infant on that breast.

Less research has been done on traditional holding in the mother's arms, but Legault and Goulet (1995) reported that, although mothers reported satisfaction with the traditional holding method, they preferred the kangaroo method because they felt closer to their infants. Bier et al. (1996) found more stability in milk production in mothers when skin-to-skin holding was used rather than the traditional method. In a study involving traditional holding, Jonsson et al. (2001) reported coregulation in affect between mothers and their 2- to 4-month-old infants who were born at term. Mothers followed behavior, facial expression, or utterance of their infants with words spoken with the same feeling, intensity, and duration as the infant activity. Thus, holding may facilitate both interactive and physiologic coregulation. In preterm infants, kangaroo holding may be more effective in promoting coregulation than the traditional method.

Antenatal corticosteroids. Antenatal corticosteroids (betamethasone or dexamethasone) given to mothers at risk of preterm labor reduce the frequency of birth complications in the infant (Caterino et al., 2001; Vermillion, Soper, Bland, & Newman, 2000). Betamethasone is the steroid most commonly administered. Mothers typically receive two doses of betamethasone in a 24-hr interval several weeks to immediately before delivery. Some research on baseline and random cortisol levels in infants suggests that the suppressive effects of antenatal steroids on HPA activity in infants do not persist longer than a few days after birth (Ballard, Gluckman, Liggins, Kaplan, & Grumbach, 1980; Kajante et al., 2004). Davis and colleagues, however, found that preterm infants of less than 1 week postnatal age, whose mothers received antenatal betamethasone up to 21 days before delivery, did not show an increase in salivary cortisol levels in response to a stressful event as did infants without betamethasone exposure (Davis et al., 2004). Long-term effects of antenatal steroids on the mother may depend on the amount of steroid given and the length of time since the last dose. McKenna and Fisk (2004) found no adrenal suppression in mothers 6 weeks after they had received one course (two doses) of betamethasone. Conversely, McKenna and colleagues reported adrenal insufficiency 3 days after the last dose in mothers who had received multiple doses of antenatal steroids (McKenna, Wittber, Nagaraja, & Samuels, 2000). If antenatal steroids affect cortisol levels of either mother or infant, the effect may interfere with HPA coregulation in the dyad.

Sound. Ambient sound may influence mother–infant cortisol levels when holding sessions are conducted in the NICU. Philbin and Evans (2006) reported that the recommended standard for operating hourly sound level in the NICU is 45 decibels (dB), yet higher levels have been reported, ranging from 55 to 120 dB (Kent, Tan, Clarke, & Bardell, 2002; Krueger, Wall, Parker, Nealis, 2005; Philbin & Gray, 2002; Robertson, Kohn, Vos, & Cooper-Peel, 1998). At sound levels greater than 55 dB, premature infants display fussiness and crying, increased heart rate and blood pressure, decreased oxygen saturation, and sleep disturbance (Beckam & Mishoe, 1982; Wharrad & Davis, 1997; Zahr & Balian, 1995). Adult women exposed to persistent environmental sound levels of 63 to 78 dB and/or sound bursts reported nervousness, intestinal complaints, colds, sleep disturbance,

and anxiety (Nivison & Endresen, 1993; Standing & Stace, 1980) and displayed impaired performance on tasks requiring focused attention (Escera, Yago, Corral, Corbera, & Nunez, 2003). Mothers who reported anxiety during holding also mentioned elevated sound levels as a deterrent to holding in the NICU (Neu, 2004). Although response to sound has not been studied simultaneously in mothers and infants, their individual responses suggest that one or both may be distressed by elevated sound levels during holding. This distress may interfere with dyadic coregulation.

Touch. Type of maternal touch also may affect maternal-infant coregulation in HPA activity. Harrison, Leeper, and Yoon (1990) reported inconsistent changes in oxygen saturation and heart rate responses to parental touch in hospitalized preterm infants. The type and amount of touch were not regulated and thus parent touch may not have been contingent with infant needs. Results of other studies involving preterm infants show that gentle contact with the caregiver's palms resting on the infant's head and abdomen for 12–15 min decreased motor activity, behavioral distress, levels of active sleep, and serum cortisol levels during the touching episodes (Harrison, Williams, Berbaum, Stem, & Leeper, 2000; Modrcin-Talbott, Harrison, Groer, & Younger, 2003). Holding that is contingent with infant needs may best facilitate interactive and physiologic coregulation between mother and infant. Contingent touch implies comforting a fussy infant with gentle patting or stroking or quietly holding a sleeping infant, as opposed to indiscriminately touching, poking, or arousing a sleeping infant or doing nothing to calm a fussy infant.

Potential Interrelationships Among Variables Influencing Maternal-Infant Coregulation

Relationships may exist among type of holding, antenatal steroids, sound level in the NICU, and maternal contingent touch. Research on cortisol levels and nurturing shows that mothers with higher cortisol levels demonstrate more affectionate and responsive behaviors with their infants than mothers with lower levels (Fleming, Steiner, & Corter, 1997). If mothers who receive antenatal steroids have adrenal insufficiency (McKenna & Fisk, 2004), they may have lower cortisol levels than mothers who do not receive steroids. It is possible that mothers who receive antenatal steroids display less contingent touch during holding than mothers who do not. Contingent maternal touch also may be influenced by the sound level in the nursery. Mothers who become anxious in response to elevated sound levels during holding (Neu, 2004; Nivison & Endresen, 1993) may become less attentive toward their infants and touch them less contingently than mothers who are less disturbed by sound. The benefits of kangaroo holding, such as intense connectedness with the infant, positive well-being, self-confidence in caring for the infant, and ability to adapt to infant cues (de Macedo et al, 2007; Feldman & Eidelman, 2003), suggest that mothers who hold kangaroo style may use more contingent touch than mothers who use traditional blanket holding. Type of holding also has potential relationships with antenatal steroids and sound levels. Mothers who do not receive antenatal steroids may perceive kangaroo holding to be a more nurturing holding method and be more likely to choose it over blanket holding. In previous research, mothers reported that noise in the nursery interfered with their willingness to hold their preterm infant using the kangaroo method while their infant was hospitalized (Neu, 2004). Mothers disturbed by noise in the nursery may choose blanket holding instead of kangaroo holding. Thus, associations may exist between contingent touch and type of holding, contingent touch and antenatal steroids, contingent touch and sound level, type of holding and antenatal steroids, and type of holding and sound level.

Potential Connections Among Characteristics of the Sample and Maternal-Infant Coregulation

Several possible characteristics of the participants have the potential to alter the cortisol responsivity of the infants or mothers. In infants, illness severity, especially respiratory disease; gestational age at birth; postnatal age; and medications influence cortisol levels. Serious illness in preterm infants is associated with lower cortisol levels in the first week of life (Hanna et al., 1997; Nykänen, Anttila, Heinonen, Hallman, & Voutilainen, 2007) and higher levels at 5–8 weeks than those observed in healthier infants (Arnold et al., 1997). Infants who require prolonged supplemental oxygen (more than 28 days) or have high ventilatory requirements and infants with chronic lung changes demonstrate lower cortisol levels than infants without oxygen needs and those who do not develop chronic lung changes (Korte,

Styne, Merritt, Wertz, & Helbock, 1996; Watterberg, Gerdes, & Cook 2001). Bolt et al. (2002) and Scott and Watterberg (1995) reported an inverse relationship between gestational age and cortisol levels in the first week of life such that infants born at an earlier gestational age have higher levels of cortisol than infants born more maturely. Other researchers have found decreasing cortisol levels from 1 to 16 weeks' postnatal age in preterm infants (Arnold et al., 1997; Heckmann et al., 2005). Postnatal age also has the potential to influence the relationship between sound level and cortisol reactivity. Infants with longer exposure to elevated sound levels may be more affected by sound than infants with less exposure, especially if they were born at an earlier gestational age. Infants who have experienced more days of holding may be better able to coregulate with their mothers than infants who have experienced fewer days of holding. In addition, medications such as steroids (Guazzo, Kirkpatrick, Goodyer, Shiers, & Herbert, 1996) and acetaminophen (Hibel, Granger, Kivlighan, & Blair, 2006) have been found to alter infant cortisol levels.

Maternal cortisol levels are increased in depression and diabetes (Boyle et al., 2007; Fruehwald-Schultes et al., 1999). Ho et al. (2007) reported that, from 36 weeks' gestation onward, mothers with preeclampsia have lower cortisol levels than healthier mothers. Parity may influence coregulation in cortisol levels because multiparity is associated with more sensitivity and better face-to-face mother–infant interaction (Zahr & Cole, 1991). It is conceivable that cortisol levels of multiparous mothers are more sensitive to those of the infant than levels of primiparous mothers. Medications reported to influence maternal cortisol levels are steroids (Guazzo et al., 1996), oral contraceptives, acetylsalicylic acid, and pure agonist opioids such as oxycodone (Hibel et al., 2006) and nicotine (Granger et al., 2007).

Methods

In this exploratory study, we examined coregulation in mother–infant HPA activity, as indicated by salivary cortisol levels measured in tandem during holding. We also examined factors influencing coregulation. The study was conducted in two NICUs in a midsized metropolitan area with a convenience sample recruited over a 12-month time period. This project was approved by the Colorado Multi-Institutional Review Board as well as the Human Subject Institutional Research Review Boards at the two hospitals.

Participants

Of the mother–infant dyads approached to participate, a total of 34 fit the enrollment criteria. For the infants, these criteria included (a) postconceptional age of 33 to 36 weeks, (b) no chromosomal anomalies, (c) no major surgery, (d) no interventricular hemorrhage, (e) no current illness, (f) no mechanical ventilation at time of data collection, and (g) no postnatal steroid medications. Criteria for the mothers were (a) no maternal drug or alcohol abuse, (b) English speaking, and (c) no postnatal steroid medications. The study was explained to eligible mothers while they visited their infants in the NICU. Mothers were given 24 hr to decide and an opportunity to ask questions before signing the consent form. Informed consent was obtained from 24 (71%) of the eligible mothers.

The score for neonatal acute physiology (SNAP; Richardson, Gray, McCormick, Workman, & Goldman, 1993) was used to assess illness of the infants at birth. The SNAP consists of 26 items that are scored as 0 = *normal* to 5 = *life threatening*. All organ systems are evaluated. The SNAP was validated on 1,643 admissions in three NICUs. It correlated with nursing workload ($r = .59$), therapeutic intensity ($r = .78$), physician mortality risk ($r = .65$), and length of stay ($r = .59$).

Data Collection

For data collection, mothers were asked to hold their infants the way they typically held them, with 14 mothers (58%) opting to use the kangaroo (skin-to-skin) method of holding and 10 using the traditional horizontal holding style with the baby dressed and wrapped in a blanket. Infants held skin-to-skin wore a hat and diaper and were placed vertically between their mother's breasts, wrapped in her blouse and covered with a blanket. A day was chosen for collection when no medical procedures were scheduled so that the infants were sleeping between feedings. In several instances, the observation and collection was rescheduled because of an unplanned procedure or examination. On the study day, mothers were invited to hold their infants for a 60-min period between 10:30 a.m. and 2:00 p.m. Infants were fed every 3 hr; the 1-hr holding time was scheduled just before the first afternoon feeding to standardize the holding condition and so that the infant's last feeding would be digested by the time of saliva collection. We scheduled infant holding and data collection for the time

period between 10:30 a.m. and 2:00 p.m. to avoid early morning high and late afternoon low levels of cortisol, which has a diurnal pattern, thus maximizing the possibility of detecting a change, especially in maternal levels. Mothers refrained from eating or drinking anything but water for 45 min before the holding periods to avoid contaminating the saliva samples.

The first author (M.N.) collected saliva from the mothers and infants once the mother first picked up her infant and again 60 min after holding began. Before the first saliva collection, infants were awakened briefly for a diaper change, undressed if the mother preferred kangaroo holding, and transferred to the mother. Saliva was collected immediately after the move to the mother. Infants opened their eyes, squirmed and grunted or whimpered for 1–2 min during the diaper change and transfer to the mother for holding. During the collection after 60 min of holding, infants squirmed briefly but did not awaken.

We described our saliva-collection procedure in detail in a previous article (Neu et al., 2007). Briefly, saliva was collected from the infants using filter paper (Whatman grade 42, 2.4 × 9 cm) that was folded in half lengthwise, placed on the infant's tongue, and angled toward the side of the infant's mouth for 30 s to 3 min until the lower 1/5 to 1/4 of the paper was completely wetted. The furthest extent of the absorption of the saliva was marked with pencil. The filter paper was dried by hanging the wet end down for 3–4 hr, and the dried paper was placed in a sealed plastic bag. Filters were stored at room temperature until assayed. For maternal saliva collection, the mother spit into a 5-ml polypropylene tube. Approximately 0.5 ml of saliva was collected and then frozen at −22°C until assayed.

Mothers sat in a recliner or rocking chair with a footrest during holding, and a folding screen was placed around the dyad for privacy. The first author (M.N.) observed the mother through a small opening in the privacy screen and recorded whether maternal touch was contingent, using 1-min time sampling throughout the 60-min observation period. Although the mothers were informed that they were being observed, they could not easily see the observer. Maternal touch was noted as contingent when it was deemed appropriate in response to the infant behavior. The rater (M.N.) was certified in Nursing Child Assessment Satellite Training (NCAST; Sumner & Spietz, 1994) and used infant stress behaviors described in NCAST as a basis for rating infant distress. The rating of contingent maternal touch was also based on NCAST maternal response to distress as well as the description of contingent touch by Kartner et al. (2007). For instance, touch was noted as contingent when the mother quietly held, rather than stimulating, a sleeping infant or consoled a fussy infant within 5 s by gently stroking or patting. The variable contingent touch was the percentage of the holding episode during which the mother engaged in appropriate touch with her infant.

Sound levels in the NICU during the holding sessions were monitored with a TES sound meter, model 1352A (TES Electrical Electronic Corp., Taipei, Taiwan), using the A-scale filter. The sound meter was calibrated immediately before the study began. The TES sound meter is accurate to ±1.5 dB, has a resolution of 0.1 dB, updates every 0.5 s, and measures between 30 and 130 dB. The meter was set on a secure table near the opening of the curtain in front of the investigator. The time and duration of sound levels exceeding 55 dB were manually recorded by the investigator. Equivalent continuous noise level (Leq) is a measurement of sound pressure (noise) level during a stated period of time that accounts for fluctuating sound levels during that period (Office of Noise Abatement and Control, 1974; Philbin, Robertson, & Hall, 1999). The variable sound level was the percentage of time during the holding session that Leq was greater than 55 dB.

Information about maternal reception of antenatal steroids was obtained from the hospital records. Mothers in this study received the standard two antenatal doses of betamethasone in a 24-hr period within 5 days of delivery.

Cortisol Extraction

The filters were extracted in assay buffer and assayed with a high-sensitivity salivary cortisol enzyme immunoassay kit (HS Salivary Cortisol EIA; Salimetrics) according to the manufacturer's directions. Whole saliva also was assayed with the EIA kit. All samples from each dyad were included on the same assay plate to minimize within-assay variance. Samples were run in duplicate. Intra- and intercoefficients of variability were less than 7% for this assay. The detection limit was 0.07 μg/dl for the extracted samples and 0.007 μg/dl for the fluid samples. Validity of the filter paper saliva collection method and details of extraction of cortisol from the filter paper have been described previously (Neu et al., 2007).

Data Analysis

The cortisol data were not normally distributed. Maternal preholding and postholding levels were $M = 4.8$ nmol/l $\pm$ 3.5, range = 16.5; and $M = 4.3$ nmol/l $\pm$ 2.7, range = 9.4, respectively. Infant preholding and postholding levels were $M = 9.6$ nmol/l $\pm$ 4.6, range = 19.5; and $M = 6.8$ nmol/l $\pm$ 4.8, range = 20.2, respectively. To achieve normality in the Time 1 to Time 2 difference ($M = 2.3$ nmol/l $\pm$ 5.6, range 22.66 nmol/l), the variables were $\log_{10}$ transformed (Munro, 2001). The absolute difference in log units between maternal and infant cortisol levels was obtained at Time 1 (baseline) and Time 2 (end of holding). A repeated measures analysis was performed to determine whether the difference in levels between members of the dyad was less at Time 2 than at Time 1 (Stevens, 2001). A smaller difference between dyad levels at Time 2 would suggest coregulation.

Multiple regression (Stevens, 2001) was performed to determine which, if any, of the four included factors (type of holding, antenatal steroids, sound level, and contingent maternal touch) influenced coregulation in HPA activity during holding. The dependent variable, coregulation in HPA activity, was obtained by subtracting the Time 2 mother–infant difference in log units from the Time 1 mother–infant difference in log units, yielding the Time 1 to Time 2 difference score in coregulation. Because "mathematically it is possible to use any level of data when calculating *r*" (Munro, 2001, p. 225), Pearson *r* was used as the measure of association between the Time 1 to Time 2 difference and all predictor variables. Sound level and contingent touch were continuous measures and type of holding and antenatal steroid use were nominal measures. Type of holding was coded 1 for kangaroo and 0 for traditional. Antenatal steroids were coded 1 if the mother received steroids before birth and 0 if she received no steroids.

The variables that showed significant univariate correlations with the Time 1 to Time 2 coregulation were then entered into a multiple regression equation as predictor variables; the smallest difference score between mothers and babies was seen as representing the most coregulation. Nunnally and Bernstein (1994) suggest using at least 10 participants per predictor in a regression equation to obtain meaningful results, so we planned to use only two predictor variables per regression. Predictor variables with obvious multicollinearity ($r > .85$) were not used in the same regression equation because their shared variance on the Time 1 to Time 2 variable would limit the size of *r*, and the importance of each predictor would be difficult to determine (Stevens, 2001).

Pearson *r* also was used to examine whether any characteristics of the sample extraneously influenced the Time 1 to Time 2 difference. Of the sample characteristics, SNAP scores, days of supplemental oxygen, gestational age at birth, and postnatal age were continuous variables. Preeclampsia, coded 1 for yes and 0 for no, and parity, coded I for multipara and 0 for primipara, were nominal variables.

Results

Participants

Data from 4 of the 24 mother–infant dyads who participated in the study were omitted from the analysis for the following reasons: (a) One mother had incomplete observational data, (b) one maternal sample was contaminated with blood, (c) one sample was missing corresponding information on whether the mother received antenatal steroids, and (d) the postholding cortisol level of one infant was below detection limits of the assay.

Of the remaining 20 dyads, 16 were recruited from a 24-bed NICU in a private hospital and 4 were recruited from a 40-bed NICU in a publicly funded hospital. None of the mothers was diagnosed with depression or uncontrolled diabetes at the time of data collection. Mothers reported taking vitamins and 3 mothers took acetaminophen within 24 hr of data collection. Acetaminophen was not mentioned by Granger et al. (2007) as a drug that influenced maternal cortisol levels. All mothers received prenatal care and all denied smoking. SNAP scores (Richardson et al., 1993) ranged from 0 to 12 ($M = 4.4 \pm 3.8$). Infants with higher SNAP scores required phototherapy and experienced respiratory difficulties and/or transient electrolyte abnormalities. Of the 20 infants, 6 required assisted ventilation for 1 to 10 days, and these along with an additional 7 infants required supplemental oxygen for 1 to 21 days ($M = 4.3 \pm 5.8$). Infants in this study were not receiving caffeine; 3 were on antibiotics. Further demographic data are presented in Table 1.

Maternal-Infant Cortisol Coregulation

The first research question in this study was, does mother–infant coregulation in HPA activity, as

Table 1. Demographic Data for Mothers and Infants ($N = 20$ dyads)

Characteristic	Frequency, *n* (%)	*M* (*SD*)
Maternal		
Age[a]		31.2 (4.2)
Ethnicity		
White	13 (65)	
Hispanic	5 (25)	
African American	2 (10)	
Illness		
Preeclampsia	10 (50)	
None	10 (50)	
Primigravida	10 (50)	
Infant		
Sex—female	9 (45)	
Gestational age at birth (weeks)[b]		31.2 (4.2)
Postconceptional age at time of cortisol sampling (weeks)[c]		34.7 (0.7)
Postnatal age at time of cortisol sampling (days)[d]		15.0 (9.0)

a. Range of maternal age = 25–35 years.
b. Range of gestational age at birth = 30–34 weeks.
c. Range of postconceptional age at time of cortisol sampling = 33–35.5 weeks.
d. Range of postnatal age at time of cortisol sampling = 5–38 days.

Table 2. Antenatal Steroids, Type of Holding, Sound Exposure, and Maternal Contingent Touch

Variable	Frequency, *n* (%)	*M* (*SD*)
Received antenatal betamethasone	10 (50)	
Type of holding		
Kangaroo	11 (55)	
Blanket	9 (45)	
Percentage of sound exposure >55 dB during observation		43.7 (23.6)
Percentage of maternal contingent touch received by infants during observation		70.0 (18.1)

indicated by salivary cortisol levels, occur during holding? The repeated measures analysis showed a significant change in the mean difference between maternal and infant cortisol from Time 1 to Time 2, Wilks's Lambda (1,19) = 5.6, $p = .029$. The mean mother–infant difference in log units of salivary cortisol levels at Time 2 ($M = .28 \pm .29$) was less than the mean difference at Time 1 ($M = .42 \pm .27$).

The second research question was, if mother–infant coregulation in HPA activity exists during holding, do the factors type of holding, antenatal steroids, sound level, and maternal touch influence this coregulation? Table 2 presents the values for these variables. The two variables most correlated with the Time 1 to Time 2 difference score were sound level and antenatal steroids (see Table 3). Although the correlation between antenatal steroids and the Time 1 to Time 2 difference scores was nonsignificant, the effect size was large (.80). These two variables were entered into the regression equation as predictor variables. The regression of the Time 1 to Time 2 coregulation on the predictor variables accounted for 39% (adjusted R^2) of the variance of coregulation and was statistically significant, $p = .006$. Sound level was the only independently significant predictor in the model ($p = .006$, B = .007, β = .591). These results indicate that there was a greater movement toward similar mother–infant salivary cortisol levels during holding when there was less elevation of sound level during the holding observation.

Correlations Between Sample Characteristics and the Time 1 to Time 2 Difference Score

The sample characteristics that we thought might influence the Time 1 to Time 2 difference score were SNAP score, days of supplemental oxygen, gestational age at birth, prenatal age in days at time of data collection, preeclampsia, and maternal parity. We found no significant correlations between these characteristics and the difference score, but the SNAP score ($r = .36$) and preeclampsia ($r = .31$) did show low correlations (Munro, 2001, p. 234), with infants who were sicker at birth and mothers with preeclampsia showing larger Time 1 to Time 2 difference scores than healthier infants and mothers. In correlation analysis, sample size influences the significance of the relationships between variables. In a large sample, very small correlations may be significant, whereas in a small sample lower correlations would not be statistically significant. Correlations above .3 in this small sample may be important even if not significant. Another way to examine the importance of the strength of a correlation is effect size. Effect sizes are categorized as .20 = *small*, .50 = *medium*, and .80 = *large*. The effect sizes were .78 for the SNAP score and .65 for preeclampsia (Munro, 2001, p. 90).

Although not primary variables of interest, the SNAP score and preeclampsia were each entered into a multiple regression equation as a predictor variable with sound level to examine whether either the SNAP score or preeclampsia contributed to the variance of

Table 3. Correlations of Predictor Variables with Time 1 to Time 2 Cortisol Difference Score and Intercorrelations Among Predictor and Extraneous Variables

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Time 1 to Time 2 mother–infant cortisol difference	—	−.09	.37	.64**	−.22	.36	.09	.31	.10	.02	.22
2. Type of holding		—	.29	.13	.55*	−.07	−.24	−.41	−.41	−.28	−.07
3. Received antenatal steroids			—	.28	−.11	.32	.14	.10	−.30	−.36	.44*
4. Percentage of elevated sound level				—	.16	.21	−.17	−.07	.02	−.15	−.19
5. Percentage of contingent touch					—	−.30	−.30	−.54*	−.28	−.28	−.32
6. SNAP						—	.54*	.36	−.12	.13	.46*
7. Days oxygen							—	.01	−.29	.14	.31
8. Preeclampsia								—	.20	.18	.09
9. Parity									—	.04	−.32
10. Gestational age at birth										—	.25
11. Postnatal age											—

*$p < .05$; **$p < .01$.

the Time 1 to Time 2 difference score. The regression of the Time 1 to Time 2 difference score on the sound level and SNAP accounted for 40% (adjusted R^2) of the variance of coregulation and was statistically significant, $p = .005$. Sound level was the only independently significant predictor in the model ($p = .005$, B = .007, β = .593). In the second analysis, the regression of the Time 1 to Time 2 difference on sound level and preeclampsia accounted for 48% (adjusted R^2) of the variance of coregulation and was statistically significant, $p = .000$. Sound level ($p = .001$, B = .007, β = .665) and preeclampsia ($p = .047$, B = .182, β = .354) were both significant predictors in the model.

Discussion

This exploratory study examined coregulation in salivary cortisol levels of mothers and preterm infants while mothers held the infants. Salivary cortisol levels of mothers and infants were significantly closer at the end of a 60-min holding session than they were before holding began, indicating coregulation in cortisol levels. A feature of behavioral coregulation is adaptation in at least one member of the dyad to accommodate or modify the behavior of the other. The amount of movement in mothers' and infants' cortisol levels toward each other during the holding session indicated adaptation of dyadic cortisol levels. Of the factors hypothesized to influence maternal-infant coregulation in cortisol levels, only the percentage of time during which the environmental sound level was greater than 55 dB was a significant predictor.

Because of the reported benefits of kangaroo holding to the infant, mother, and the mother–infant relationship (Affonso et al., 1993; Chwo et al. 2002; Feldman et al., 2002; Ludington-Hoe et al.,1999; Neu, 1999; Rojas et al., 2003) and the close physical contact between mother and infant during that method of holding, it was surprising that the kangaroo method was not associated with greater maternal-infant cortisol coregulation in univariate analysis. Most research focusing on kangaroo holding compares kangaroo holding to infants lying in their beds or to "standard care" (Chwo et al., 2002; deMacedo et al., 2007; Feldman et al., 2002; Rojas et al., 2003). Perhaps, the extra attention received by mothers holding kangaroo style that was not given to mothers in standard care in these studies also facilitated positive mother–infant interaction. Although blanket holding has been studied far less than kangaroo holding, Jonsson et al. (2001) reported coregulation in mother–infant dyads during traditional holding, suggesting that kangaroo and traditional holding may provide similar benefits to dyads. In a randomized controlled trial comparing kangaroo with traditional holding, researchers found no differences between groups in behavior or development in infants, or in depression, anxiety, or lactation in mothers (Miles, Cowan, Glover, Stevenson, & Modi, 2006). Another possibility for the lack of association between kangaroo holding and cortisol coregulation is that confounding environmental and/or medical factors such as elevated sound level affects some physiologic indicators more than type of holding does.

The results of this study are consistent with others that have used physiologic measures such as vagal-tone maturation (Smith, 2003) or salivary cortisol (Mooncey Giannakoulopoupos, Glover, Acolet, & Modi, 1997) to compare the effects of kangaroo holding to those of infants lying in bed and have found no differences. However, it is still possible that cortisol levels would show a differential pattern related to holding if measured longitudinally and after a period of time in the home environment. It is also important to note that the low power in this study precludes detection of anything less than moderate effects (Munro, 2001, p. 82).

Use of antenatal steroids was the second variable we hypothesized would influence mother–infant HPA coregulation during holding. Receipt of antenatal steroids correlated with less movement toward similar salivary cortisol levels during holding, suggesting there was less maternal-infant cortisol coregulation in dyads where mothers received antenatal steroids. The large Cohen's *d* effect size (0.8) indicates that suppressive effects of antenatal steroids on HPA activity, as found by Davis et al. (2003) in infants, interfered with cortisol coregulation in mother and infants. Antenatal steroids, however, had no predictive value on maternal-infant cortisol coregulation when sound level was also included in the regression analysis. Although steroid use did not account for any variance beyond what it shared with sound level, antenatal steroid use is a factor to consider when examining cortisol levels in the first weeks after delivery.

Sound level during holding was the third factor we hypothesized would influence mother–infant cortisol coregulation. Exposure to sound levels greater than 55 dB during holding was the only factor that independently predicted coregulation in mother–infant cortisol levels during holding. The types of environmental sound in this study were similar to those reported by others (Kent et al., 2002; Krueger et al., 2005; Robertson et al., 1998), such as conversation by health care personnel, monitor alarms, ringing telephones, crying infants, and those related to problems with infants in nearby beds. Mothers often held their infants in busy areas of the nursery. It was beyond the scope of this study to examine directionality of cortisol levels of mothers or infants in response to sound level. Prior research suggests that either mothers or infants may have been stressed by elevated sound levels during holding (Escera et al., 2003; Nivison & Endresen, 1993; Wharrad & Davis, 1997; Zahr & Balian, 1995). This stress may have increased cortisol levels of either member of the dyad, increasing the difference score.

One concern about elevated sound levels in the nursery is that the background sound may exceed the sound intensities of maternal speech. In this study, mothers appropriately held their infants without speaking during the observations because the infants typically were sleeping. However, when mothers do speak to their alert infants while holding them, background noise may keep infants from hearing the sound of their mothers' voices or the words may be unintelligible (Philbin et al., 1999). In utero the fetus is exposed to the mother's voice, and the infant born at term demonstrates the ability to discriminate the mother's voice at birth (Hepper, Scott, & Shahidullah, 1993). Infants born preterm who cannot hear the mother's voice because of elevated background sound in the NICU may be at risk of mother–infant attachment difficulties. Larger studies to further investigate sound level as a potential impediment to the mother–infant relationship during hospitalization are warranted.

The fourth factor we hypothesized would influence mother–infant cortisol coregulation was contingent touch. The gentle pressure of the mother's body during holding seems similar to the gentle pressure of parental touch that has been found to decrease cortisol levels in infants who were lying in their beds (Modcrin-Talbott et al.). Contingent touch in this study was defined as a mother quietly holding a sleeping infant or consoling a fussy infant by gently stroking or patting. Observational bias is a possibility, as the researcher evaluated maternal touch during holding. In future research, videotaping the observation with subsequent recording of dyad behaviors by blinded coders would eliminate possible bias. Another possibility that might account for lack of association between maternal contingent touch and cortisol coregulation, which can be addressed in future research, is that the sound levels in this study might have overridden any effects of maternal contingent touch. Perhaps, contingent touch in a quiet environment would positively influence cortisol coregulation in the dyad. It is important to note that moderate coregulation was observed just from the experience of holding. Contingent touch did not significantly amplify or detract from the overall effect of holding.

Intercorrelations between the predictor variables revealed a significant and moderate positive correlation between contingent touch and type of holding. Mothers who used the kangaroo holding method demonstrated more contingent touch than mothers who used the blanket method of holding. Mothers

may be less likely to attempt interaction with a sleeping infant when they cannot see the baby's face, as occurs in kangaroo holding. Feelings of well-being and connectedness with the infant described in other studies of kangaroo holding (de Macedo et al., 2007; Feldman & Eidelman, 2003) may also have lessened mothers' need to inappropriately arouse their infants. This intercorrelation did not affect our primary analysis, however, because neither type of holding nor contingent touch was used in that analysis.

Most sample characteristics showed very low or no correlation with coregulation. Higher correlations were found with infant illness (SNAP score) and maternal preeclampsia. Infants and mothers who were ill at birth were less able to respond to the other member of the dyad than more healthy infants and mothers. These results are similar to reports of effects of illness on cortisol levels in infants (Hanna et al., 1997; Watterberg et al., 2001) and mothers (Ho et al., 2007). However, when coupled with sound level as a predictor in the regression equation, only maternal preeclampsia added variance in the model. The SNAP score shared some variance with sound level, while preeclampsia did not, which is the most probable explanation for the lack of significance of the SNAP score. In the findings reported by Ho et al. (2007), maternal cortisol levels in preeclampsia were not lower than those of healthier mothers until 36 weeks' gestation. Mothers in this study gave birth before 36 weeks. The effect of preeclampsia on HPA activity seems to persist postnatally.

Responsivity of cortisol levels between mothers and infants was not affected by days on oxygen, gestational age at birth, or postnatal age. Korte et al. (1996) and Watterberg et al. (2001) reported lower cortisol levels in infants who required oxygen for more than 28 days and displayed chronic lung changes. The infants in the current study did not require oxygen longer than 21 days and so may not have developed lung disease serious enough to interfere with the dyads' coregulation. In previous studies cortisol levels were influenced by gestational and postnatal age (Arnold et al., 1997; Bolt et al., 2002; Korte et al., 1996; Scott & Watterberg, 1995; Watterberg et al., 2001). These studies included infants born at less than 28 weeks' gestational age. The infants in the current study were at least 30 weeks' gestation at birth and were at least 32 weeks' postconceptional age when the study was conducted. Perhaps, cortisol levels of older infants are less affected by age than those of very-small-for-gestational-age infants. Cortisol responsivity was not assessed in the aforementioned studies. Infants may have lower cortisol levels but still be able to respond to their mothers' cortisol levels.

Our supposition that maternal parity would affect a dyad's ability to physiologically coregulate was based on the studies of face-to-face coregulation reported by Zahr and Cole (1991). The very low correlation found between the Time 1 to Time 2 difference scores and parity in this study suggests that parity does not affect cortisol coregulation and that sensitivity to the other dyadic member's cortisol levels may depend on a different mechanism of maternal sensitivity than that found in face-to-face interactions.

Conclusion

This research examined neuroendocrine relationships between mothers and their preterm infants during holding, which is the primary early activity between a mother and her infant. Based on our results, a coregulatory relationship, as indicated by salivary cortisol levels, appears to exist between mothers and infants during holding. The degree of coregulation was influenced by sound levels, with dyads being more likely to demonstrate coregulation in HPA activity when sound levels were low. Thus, nurses in the NICU can facilitate the mother–infant relationship by promoting a quiet environment around mothers who are holding their infants.

Assessment of the quality of the mother–child interactive experience in the NICU is an area for future research. Using more than two salivary cortisol measures during the holding observation in future studies would provide more information about how the dyad coregulates physiologically. Future research with large samples addressing the complexities of examining coregulation in cortisol in mother–infant dyads, the benefits of physiologic coregulation, and the association between mother–infant face-to-face interaction and physiologic coregulation is needed.

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References

Aardel, E., & Holm, A. C. (1995). Cortisol in saliva—reference ranges and relation to cortisol in serum. *European Journal of Clinical Chemistry and Clinical Biochemistry*, *33*, 927-932.

Affonso, D., Bosque, E., Wahlberg, V., & Brady, J. (1993). Reconciliation and healing for mothers through skin-to-skin contact provided in an American tertiary level intensive care nursery. *Neonatal Network*, *12*, 25-32.

Arnold, J., Leslie, G., Bowen, J., Watters, S., Kreutzmann, D., & Silink, M. (1997). Longitudinal study of plasma cortisol and 17-hydroxyprogesterone in very-low-birth-weight infants during the first 16 weeks of life. *Biology of the Neonate*, *72*, 148-155.

Ballard, P. L., Gluckman, P. D., Liggins, G. C., Kaplan, S. L., & Grumbach, M. M. (1980). Steroid and growth hormone levels in premature infants after prenatal betamethasone therapy to prevent respiratory distress syndrome. *Pediatric Research*, *14*, 122-127.

Beckham, R. W., & Mishoe, S. C. (1982). Sound levels inside incubators and oxygen hoods used with nebulizers and humidifiers. *Respiratory Care*, *27*, 33-40.

Bier, J. A., Ferguson, A. E., Morales, Y., Liebling, J. A., Archer, D., Oh, W., et al. (1996). Comparison of skin-to-skin contact with standard contact in low-birth-weight infants who are breast-fed. *Archives of Pediatric and Adolescent Medicine*, *150*, 1265-1269.

Bolt, R. J., vanWeiddenbruch, M. M., Popp-Snijders, C., Sweep, F. G. J., Lafeber, H. N., & Delemarre-van de Waal, H. A. (2002). Maturity of the adrenal cortex in very preterm infants is related to gestational age. *Pediatric Research*, *52*, 405-410.

Bornstein, M., & Suess, P. (2000). Child and mother cardiac vagal tone: Continuity, stability, and concordance across the first 5 years. *Developmental Psychology*, *36*, 54-65.

Boyle, S. H., Surwit, R. S., Georgiades, A., Brummett, B. H., Helms, M. J., Williams, R. B., et al. (2007). Depressive symptoms, race, and glucose concentrations: The role of cortisol as mediator. *Diabetes Care*, *30*, 2484-2488.

Calixto, C., Martinez, F. E., Jorge, S. M., Moreira, A. C., & Martinelli, C. E. (1995). Correlation between plasma and salivary cortisol levels in preterm infants. *Journal of Pediatrics*, *140*, 116-118.

Caterino, J., Verma, U., Visintainer, P., Eliman, A. Klein, S. A., & Tejani, N. (2001). Antenatal steroids and neonatal periventricular leukomalacia. *Obstetrics and Gynecology*, *97*, 135-139.

Chwo, M. J., Anderson, G. C., Good, M., Dowling, D. A., Shiau, S. H., & Chu, D. M. (2002). A randomized controlled trial of early kangaroo care for preterm infants: Effects on temperature, weight, behavior, and acuity. *Journal of Nursing Research*, *10*, 129-142.

Davis, E. P., Townsend, E. L., Gunnar, M. R., Gorgieff, M. K., Guiang, S. F., Ciffuentes, R. F., & et, al. (2004). Effects of prenatal betamethasone exposure on regulation of stress physiology in healthy premature infants. *Psychoneuroendocrinology*, *29*, 1028-1036.

de Macedo, E. C., Cruvinel, F., Lukasova, K., & D'Antino, M. E. (2007). The mood variation in mothers of preterm infants in kangaroo mother care and conventional incubator care. *Journal of Tropical Pediatrics*, *53*, 344-346.

de Weerth, C., Zijl, R. H., & Buitelaar, J. K. (2003). Development of cortisol circadian rhythm in infancy. *Early Human Development*, *73*, 39-52.

Escera, C., Yago, E., Corral, M. J., Corbera, S., & Nunez, M. I. (2003). Attention capture by auditory significant stimuli: Semantic analysis follows attention switching. *European Journal of Neuroscience*, *18*, 2408-2412.

Feldman, R. (2006). From biological rhythms to social rhythms: Physiological precursors of parent-infant synchrony. *Developmental Psychology*, *42*, 175-188.

Feldman, R., & Eidelman, A. I. (2003). Skin-to-skin contact (kangaroo care) accelerates autonomic and neurobehavioural maturation in preterm infants. *Developmental Medicine and Child Neurology*, *45*, 274-281.

Feldman, R., Eidelman, A. I., & Rotenberg, N. (2004). Parenting stress, infant emotion regulation, maternal sensitivity, and the cognitive development of triplets. A model for parent and child influences in a unique ecology. *Child Development*, *75*, 1774-1791.

Feldman, R., Eidelman, A. I., Sirota, L., & Weller, A. (2002). Comparison of skin-to-skin (kangaroo) and traditional care: Parenting outcomes and preterm infant development. *Pediatrics*, *110*, 16-26.

Feldman, R., Weller, A., Sirota, L., & Eidelman, A. I. (2002). Skin-to-skin contact (kangaroo care) promotes self-regulation in premature infants: Sleep-wake cyclicity, arousal modulation, and sustained exploration. *Developmental Psychology*, *38*, 194-207.

Fleming, A. S., Steiner, M., & Corter, C. (1997). Cortisol, hedonics, and maternal responsiveness in human mothers. *Hormones and Behavior*, *32*, 85-98.

Fogel, A. (1993). *Developing through relationships*, London: Harvester Wheatsheaf.

Fogel, A., & Garvey, A. (2007). Alive communication. *Infant Behavior and Development*, *30*, 251-257.

Fruehwald-Schultes, B., Kern, W., Borg, W., Wellhoener, P., Kerner, W., Born, J., et al. (1999). Supraphysiological hyperinsulinemia acutely increases hypothalamic-pituitary-adrenal secretory activity in humans. *Journal of Clinical Endocrinology and Metabolism*, *84*, 3041-3046.

Granger, D. A., Blair, C., Willoughby, M., Kivlighan, K. T., Hibel, L. C., Fortunato, C. K., et al. (2007). Individual differences in salivary cortisol and alpha amylase in

mothers and their infants: Relation to tobacco smoke exposure. *Developmental Psychobiology*, *49*, 692-701.

Guazzo, E. P., Kirkpatrick, P. J., Goodyer, I. M., Siers, H. M., & Herbert, J. (1996). Cortisol, dehydroepiandrosterone (DHEA), and DHEA sulfate in the cerebrospinal fluid of man: Relation to blood levels and the effects of age. *Journal of Clinical Endocrinology & Metabolism*, *81*, 3951-3960.

Gunnar, M. R., Brodersen, L., Nachmias, M., Buss, K., & Rigatuso, J. (1996). Stress reactivity and attachment security. *Developmental Psychobiology*, *29*, 191-204.

Hanna, C. E., Jett, P. L., Laird, M. R., Mandel, S. H., LaFranchi, S. H., & Reynolds, J. W. (1997). Corticosteroid binding globulin, total serum cortisol, and stress in extremely low birth-weight infants. *American Journal of Perinatology*, *14*, 201-204.

Harrison, L. L, Leeper, J. D., & Yoon, M. (1990). Effects of early parent touch on preterm infants' heart rates and arterial oxygen saturation levels. *Journal of Advanced Nursing*, *15*, 877-885.

Harrison, L. L., Williams, A. K., Berbaum, M. L., Stem, J. T., & Leeper, J. (2000). Physiologic and behavioral effects of gentle human touch on preterm infants. *Research in Nursing & Health*, *23*, 435-446.

Heckmann, M., Hartmann, M. F., Kampschulte, B., Gack, H., Bodeker, R. H., Gortner, L., et al. (2005). Cortisol production rates in preterm infants in relation to growth and illness: A noninvasive prospective study using gas chromatography-mass spectrometry. *Journal of Clinical Endocrinology and Metabolism*, *90*, 5737-5742.

Hepper, P. G., Scott, D., & Shahidullah, S. (1993). Newborn and fetal response to maternal voice. *Journal of Reproductive and Infant Psychology*, *11*, 147-153.

Hibel, L. C., Granger, D. A., Kivlighan, K. T., & Blair, C. (2006). Individual differences in salivary cortisol: Associations with common over-the-counter and prescription medication status in infants and their mothers. *Hormones and Behavior*, *50*, 293-300.

Ho, J. T., Lewis, J. G., O'Loughlin, P., Bagley, C. J., Romero, R., & Dekker, G. A, et al. (2007). Reduced maternal corticosteroid-binding globulin and cortisol levels in pre-eclampsia and gamete recipient pregnancies. *Clinical Endocrinology*, *66*, 869-877.

Hui-Chin, H., & Fogel, A. (2003). Stability and transitions in mother–infant face-to-face communication during the first 6 months: A microhistorical approach. *Developmental Psychology*, *39*, 1061-1082.

Isabella, R. A., & Belsky, J. (1991). Interactional synchrony and the origins of infant-mother attachment: A replication study. *Child Development*, *62*, 373-384.

Jaffe, J., Beebe, B., Feldstein, S., Crown, C. L., & Jasnow, M. D. (2001). Rhythms of dialogue in infancy: Coordinated timing in development. *Monographs of the Society for Research in Child Development*, *66*, i-viii, 1-132.

Jonsson, C. O., Clinton, D. N., Fahrman, M., Mazzaglia, G., Novak, S., & Sorhus, K. (2001). How do mothers signal shared feeling states to their infants? An investigation of affect attunement and imitation during the first year of life. *Scandinavian Journal of Psychology*, *42*, 377-381.

Kajante, E., Raivio, T., Janne, O. A., Hovi, P., Dunkel, L., & Andersson, S. (2004). Circulating glucocorticoid bioactivity in the preterm newborn after antenatal betamethasone treatment. *Journal of Clinical Endocrinology & Metabolism*, *89*, 3999-4003.

Karger, R. H. (1979). Synchrony in mother–infant interaction. *Child Development*, *50*, 882-885.

Kartner, J., Keller, H., Lamm, B., Abels, M., Yovsi, R. D., Chaudhary, N., et al. (2007). Similarities and differences in contingency experiences of 3-month-olds across sociocultural contexts. *Infant Behavior and Development*, *31*, 488-500.

Kent, W. D., Tan, A. K., Clarke, M. C., & Bardell, T. (2002). Excessive noise levels in the neonatal ICU: Potential effects on auditory system development. *Journal of Otolaryngology*, *31*, 355-360.

Kirschbaum, C., & Hellhammer, D. H. (1989). Salivary cortisol in psychobiological research: An overview. *Neuropsychobiology*, *22*, 150-169.

Korte, C., Styne, D., Merritt, T. A., Wertz, A., & Helbock, H. J. (1996). Adrenocortical function in the very low birth weight infant: Improved testing sensitivity with neonatal outcome. *Journal of Pediatrics*, *128*, 257-263.

Krueger, C., Wall, S., Parker, L., & Nealis, R. (2005). Elevated sound levels within a busy NICU. *Neonatal Network*, *24*, 33-37.

Laudenslager, M. L., Bettinger, T., & Sackett, G. (2006). Saliva as a medium for assessing cortisol and other compounds in nonhuman primates: Collection assay, and examples. In G. Sackett, & G. Ruppenthal (Eds.), *Nursery rearing of nonhuman primates in the 21st century* (pp. 403-428). New York: Plenum.

Laudenslager, M., Boccia, M., Berger, C., Gennero-Ruggles, N., & McFerran, B, & Reite, M. (1995). Total cortisol, free cortisol, and growth hormone associated with brief social separation experiences in young macaques. *Developmental Psychobiology*, *28*, 199-211.

Lester, B. M., Hoffman, J., & Brazelton, T. B. (1985). The rhythmic structure of mother–infant interaction in term and preterm infants. *Child Development*, *56*, 15-27.

Legault, M, & Goulet, C. (1995). Comparison of kangaroo and traditional methods of removing preterm infants from incubators. *Journal of Obstetric, Gynecologic and Neonatal Nursing*, *24*, 501-506.

Liu, D., Diorio, J., Tannenbaum, B., Caldji, C., Francis, D., Freedman, A., et al. (1997). Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. *Science*, *277*, 1659-1662.

Ludington-Hoe, S. M., Anderson, G. C., Simpson, S., Hollingshead, A., Argote, L., & Rey, H. (1999). Birth-related fatigue in 34-35 week preterm neonates: Rapid recovery with very early kangaroo (skin-to-skin) care.

Journal of Obstetric, Gynecologic, & Neonatal Nursing, *28*, 94-103.

Ludington-Hoe, S. M., Lewis, T., Morgan, K., Cong, X., Anderson, L., & Reese, S. (2006). Breast and infant temperatures with twins during shared kangaroo care. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, *35*, 223-231.

McKenna, D. S., & Fisk, A. D. (2004). The effect of a single course of antenatal corticosteroids on maternal adrenal function at term. *Journal of Maternal-Fetal & Neonatal Medicine*, *16*, 33-36.

McKenna, D. S., Wittber, G. M., Nagaraja, H. N., & Samuels, P. (2000). The effects of repeat doses of antenatal corticosteroids on maternal adrenal function. *American Journal of Obstetrics & Gynecology*, *183*, 669-673.

Meaney, M. J., Aitken, D. H., van Berkel, C., Bhatnagar, S., & Sapolsky, R. M. (1988). Effect of neonatal handling on age-related impairments associated with the hippocampus. *Science*, *239*(4841, Pt. 1), 766-768.

Miles, R., Cowan, F., Glover, V., Stevenson, J., & Modi, N. (2006). A controlled trial of skin-to-skin contact in extremely preterm infants. *Early Human Development*, *82*, 447-455.

Modrcin-Talbott, M. A., Harrison, L. L., Groer, M. W., & Younger, M. S. (2003). The biobehavioral effects of gentle human touch o preterm infants. *Nursing Science Quarterly*, *16*, 60-67.

Mooncey, S., Giannakoulopoupos, X., Glover, V., Acolet, D., & Modi, N. (1997). The effect of mother–infant skin-to-skin contact on plasma cortisol and B-endorphin concentrations in preterm newborns. *Infant Behavior and Development*, *20*, 553-557.

Morelius, E., Theodorsson, E., & Nelson, N. (2004). Salivary cortisol and mood and pain profiles during skin-go-skin care for an unselected group of mothers and infants in neonatal intensive care. *Pediatrics*, *166*, 1105-1113.

Munro, B. H. (2001). *Statistical methods for health care research*, (4th ed.). New York: Lippincott.

Neu, M. (2004). Kangaroo care: Is it for everyone? *Neonatal Network*, *23*, 47-54.

Neu, M. (1999). Parents' perception of skin-to-skin care with their preterm infants requiring assisted ventilation. *Journal of Obstetric, Gynecologic and Neonatal Nursing*, *28*, 1-8.

Neu, M., Goldstein, M., Gao, D., & Laudenslager, M. L. (2007). Salivary cortisol in preterm infants: Validation of a simple method for collecting saliva for cortisol determination. *Early Human Development*, *83*, 47-54.

Nivison, M. E., & Endresen, I. M., (1993). An analysis of relationships among environmental noise, annoyance and sensitivity to noise, and the consequences for health and sleep. *Journal of Behavioral Medicine*, *16*, 257-276.

Nunnally, J. C., & Bernstein, I. (1994). *Psychometric theory*, (3rd ed.). St Louis, Donnally & Sons.

Nykänen, P., Anttila, E., Heinonen, K., Hallman, M., & Voutilainen, R. (2007). Early hypoadrenalism in premature infants at risk for bronchopulmonary dysplasia or death. *Acta Paediatrica*, *96*, 1600-1605.

Office of Noise Abatement and Control, U.S. Environmental Protectio Agency. Information on levels of environmental noise requisite to protect public health and welfare with an adequate margin of safety. (Report No. 550/0-74-00,1974. p. 20-23, 30, A-5, D-2).

Philbin, M. K., & Evans, J. B. (2006). Standards for the acoustic environment of the newborn ICU. *Journal of Perinatology*, *26*(Suppl. 3), S27-S30.

Philbin, M. K., & Gray, L. (2002). Changing levels of quiet in an intensive care nursery. *Journal of Perinatology*, *22*, 455-460.

Philbin, M. K., Robertson, A., & Hall, J. W. (1999). Recommended permissible noise criteria for occupied, newly constructed or renovated hospital nurseries. *Journal of Perinatology*, *19*(Pt. 1), 559-563.

Richardson, D., Gray, J., McCormick, M., Workman, K., & Goldman, D. (1993). Score for neonatal acute physiology: A physiologic severity index for neonatal intensive care. *Pediatrics*, *91*, 617-623.

Robertson, A., Kohn, J., Vos, P., & Cooper-Peel, C. (1998). Establishing a noise measurement protocol for neonatal intensive care units. *Journal of Perinatology*, *18*, 126-130.

Rojas, M. A., Kaplan, M., Quevedo, M., Sherwonit, E., Foster, L. B., Ehrenkranz, R. A., et al. (2003). Somatic growth of preterm infants during skin-to-skin care versus traditional holding: A randomized, controlled trial. *Journal of Developmental and Behavioral Pediatrics*, *24*, 163-168.

Scott, S. M., & Watterberg, K. L. (1995). Effect of gestational age, postnatal age and illness on plasma cortisol concentrations in premature infants. *Pediatric Research*, *37*, 112-116.

Smith, S. L. (2003). Heart period variability of intubated very-low-birth-weight infants during incubator care and maternal holding. *American Journal of Critical Care*, *12*, 54-64.

Standing, L., & Stace, G. (1980). The effects of environmental noise on anxiety level. *Journal of General Psychology*, *103*, 263-272.

Stern, D. N., Hofer, L., Haft, W., & Dore, J. (1985). Affect attunement: The sharing of feeling states between mother and infant by means of intermodal fluency. In T. M. Field, & N. A. Fox (Eds.), *Social perception in infants*, New York: Basic Books.

Stevens, J. (2001). *Applied multivariate statistics for the social sciences* (4th ed.). New Jersey: Erlbaum & Associates.

Sumner, G., & Spietz, A. (1994). *NCAST caregiver/parent-child interaction feeding manual*, Seattle: NCAST Publications, University of Washington, School of Nursing.

Tronick, E. Z., & Cohn, J. F. (1989). Infant-mother face-to-face interaction: Age and gender differences in

coordination and the occurrence of miscoordination. *Child Development*, *60*, 85-92.

Tu, M. T., Grunau, R. E., Petrie-Thomas, J., Haley, D. W., & Whitfield, M. F. (2007). Maternal stress and behavior modulate relationships between neonatal stress, attention, and basal cortisol at 8 months in preterm infants. *Developmental Psychobiology*, *49*, 150-164.

Watterberg, K. L., & Scott, S. M. (1995). Evidence of early adrenal insufficiency in babies who develop bronchopulmonary dysplasia. *Pediatrics*, *95*, 120-125.

Watterberg, K. L., Gerdes, J. S., & Cook, K. L. (2001). Impaired glucocorticoid synthesis in premature infants developing chronic lung disease. *Pediatric Research*, *50*, 190-195.

Wharrad, H. J., & Davis, A. C. (1997). Behavioral and autonomic responses to sound in pre-term and full-term babies. *British Journal of Audiology*, *31*, 315-329.

Vermillion, S., Soper, D. E., Bland, M. L., & Newman, R. B. (2000). Effectiveness of antenatal cortiscosteroid administration after preterm premature rupture of the membranes. *Obstetrics and Gynecology*, *183*, 925-929.

Zahr, L. K., & Balian, S. (1995). Responses of premature infants to routine nursing interventions and noise in the NICU. *Nursing Research*, *44*, 179-185.

Zahr, L., & Cole, J. (1991). Assessing maternal competence and sensitivity to premature infants' cues. *Issues in Comprehensive Pediatric Nursing*, *14*, 231-240.