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Direct and Indirect Effects of Breast Milk on the Neurobehavioral and Cognitive Development of Premature Infants

ABSTRACT: *Eighty-six premature infants were tested to examine the effects of maternal breast milk on infant development. Infants were classified by breast-milk consumption during the hospitalization period (M = 57.4 days) into three groups: those receiving minimal (<25% of nutrition), intermediate (25–75%), and substantial (>75%) amounts of breast milk. Infants in the three groups were matched for birth weight, gestational age (GA), medical risk, and family demographics. At 37 weeks GA, mother–infant interaction was videotaped, maternal depression self-reported, and neurobehavioral maturation assessed by the Neonatal Behavior Assessment Seale (Brazelton, 1973). At 6 months corrected age, infants were tested with the Bayley II (Bayley, 1993). Infants receiving substantial amounts of breast milk showed better neurobehavioral profiles—in particular, motor maturity and range of state. These infants also were more alert during social interactions, and their mothers provided more affectionate touch. Higher maternal depression scores were associated with lower quantities of breast milk, longer latencies to the first breast-milk feeding, reduced maternal affectionate touch, and lower infant cognitive skills. Maternal affectionate touch moderated the relations between breast milk and cognitive development, with infants receiving a substantial amount of breast milk and frequent touch scoring the highest. In addition to its nutritional value, breast milk may be related to improved maternal mood and interactive behaviors, thereby indirectly contributing to development in premature infants.*
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Whether breastfeeding exerts a lasting impact on children's development has been an unresolved controversy for several decades (Jain, Concato, & Leventhal, 2002). Several large-scale studies demonstrated that children who were breast-fed as infants scored higher on IQ tests in childhood and adolescence (Johnson, Swank, Howie, Baldwin, & Owen, 1996; Mortensen, Michaelsen, Sanders, & Reinisch, 2002; Quinn et al., 2001). Critics, on the other hand, have argued that nursing mothers differ from their nonnursing peers on a range of sociodemographic variables; they are older, more educated, and have a more supportive social network (Furman, Minich, & Hack, 1998; Lucas et al., 1998). Once sociodemographic factors were controlled, the effect of breastfeeding on intelligence was attenuated, suggesting that environmental conditions, not breast milk, per se, are the decisive factors in shaping infant development (Gale

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& Martyn, 1996; Jacobson, Chiodo, & Jacobson, 1999; Richards et al., 1998). In a recent comprehensive review of the literature from 1929 to the present, Jain and colleagues (2002) critically examined each study according to seven methodological criteria such as sample size, quality of feeding data, or blinding. Only two studies fulfilled all criteria—one discovered an effect for breast-feeding on later IQ whereas the other did not—emphasizing the need to further explore the mechanisms that link breast milk and development. Two potential mechanisms have been proposed (Quinn et al., 2001). The first considers the nutritional content of breast milk and its direct impact on complex neural and cognitive functioning (Larque, Demmelmair, & Koletzko, 2002); the second addresses the positive effect of breast-feeding on the mother–infant relationship, thereby indirectly supporting cognitive growth. However, whereas much research examined the links between breast milk and cognitive development, regrettably little is known about its contribution to the mother–infant relationship, with minimal research assessing concrete patterns of mother–infant interaction (Golding, Rogers, & Emmett, 1997).

In contrast to the debate on the contribution of breast-feeding to development among full-term infants, evidence for the positive effects of breast milk on the cognitive development of preterms is more conclusive (Bier, Oliver, Ferguson, & Vohr, 2002; Horwood, Darlow, & Mogridge, 2001; Lucas, Morley, Cole, Lister, & Leeson-Payne, 1992; Schanler, Hurst, & Lau, 1999). Breast milk is the optimal nutrition for the premature infant as it consists of unique amounts and types of proteins, enzymes, micronutrients, lipids, and particularly long-chain polyunsaturated fatty acids, which are critical for growth and development (Heird, 2001; Koletzko et al., 2001; Larque et al., 2002). Additionally, breast milk supports the vulnerable premature infant by reducing the risk of infection and improving gastrointestinal function and the absorption of nutrients (Boersma & Lanting, 2000; Feist, Berger, & Speer, 2000; Orzalesi, 1987). Unfortunately, premature infants who would most benefit from breast milk often receive less such milk compared to full-term infants, placing them at even a higher risk (Killersreiter, Grimmer, Buhrer, Dudenhausen, & Oblade, 2002).

The mother–infant relationship following premature birth has been described as less optimal compared to infants born at term. The initial mother–infant separation, the infant's medical condition and uncertain survival, and the short pregnancy that interferes with the mother's preparation for motherhood and familiarity with the specific child often disrupt the development of maternal behavior (Feldman, Weller, Leckman, Kvint, & Eidelman, 1999). In addition, mothers of preterm infants typically experience higher levels of anxiety and depression (Brooten et al., 1988), which may further impede the development of the mother–infant relationship. During interactions, mothers of premature infants demonstrate lower levels of sensitivity and higher intrusiveness (Greene, Fox, & Lewis, 1983; Minde, 2000), and naturalistic observations show significantly less mother–infant touch and contact in the home (Davis & Thoman, 1988). Premature infants have difficulties in maintaining visual attention during play (Eckerman, Hsu, Molitor, Leung, & Goldstein, 1999), and their emotional expressions are often unclear (Malatesta, Grigoryev, Lamb, Albin, & Culver, 1986). The infant's reduced self-regulation combined with decreased maternal sensitivity and contact possibly contribute to the lower level of synchrony observed between mothers and premature infants (Lester, Hoffman, & Brazelton, 1985). Interestingly, intervention programs that facilitate maternal–infant touch and contact in the neonatal period, such as skin-to-skin contact, were found to promote interactive behavior in terms of increased maternal touch and adaptation and higher infant visual alertness, which in turn predicted better cognitive outcomes among the treated infants (Feldman, Eidelman, Sirota, & Weller, 2002). Breast-feeding has been shown to increase maternal responsiveness to her infant's cues during a feeding session (Brandt, Andrews, & Kvale, 1998) and may thus similarly facilitate more optimal mother–infant interaction patterns, possibly leading to higher cognitive outcomes.

In addition to its psychological effect, milk provision possibly affects the psychobiology of maternal behavior. Prolactin and oxytocin, which are directly involved in the production and the reflex release of breast milk (Newton, 1992), have been implicated in a range of maternal behavior across a variety of mammalian species, and possibly play a role in the initiation of maternal behavior and stress management in humans (Grattan et al., 2001; Insel, 1997; Nelson & Panksepp, 1998). Mother–infant touch and contact have been shown to stimulate oxytocin release. Newborn infants placed on the mother's chest stimulate oxytocin release by hand movement and suckling (Matthiesen, Ransjo-Arvidson, Nissen, & Uvnas-Moberg, 2001), and mother–infant skin-to-skin contact immediately after birth elevates maternal oxytocin levels (Nissen, Lilja, Widstrom, & Uvnas-Moberg, 1995). Oxytocin release may result from breast stimulation and is not solely dependent on the sucking of the infant. For instance, oxytocin increase was observed following breast massage in lactating women (Yokoyama, Ueda, Irahara, & Aono, 1994), and a comparable increase in oxytocin was found following breast pumping and breast-feeding (Zinaman, Hughes, Queenan, Labobok, & Albertson, 1992). In addition, oxytocin functions to reduce depression and anxiety, and lactating mothers were found to experience less stress compared to nonlactating mothers (Carter & Altemus, 1997; Uvnas-Moberg, 1998).

The oxytocin-mediated system is theorized to function as a feedback loop; mother–infant contact or breast stimulation stimulates oxytocin release, which in turn affects maternal mood and behavior (Carter, 1998; Insel, 1992). Following premature birth, the natural functioning of the system is likely to be disregulated. Premature birth truncates the normal duration of pregnancy and interferes with priming processes of prolactin and oxytocin secretion and binding that occur in the last trimester of pregnancy (Grattan et al., 2001). We thus hypothesize that given such a feedback loop, improvement in one component (i.e., the expression of breast milk) would be related to improvements in other components, such as increased maternal touch and reduced depression.

In sum, the present study examined the contribution of breast milk to the cognitive and neurobehavioral development of low-birth-weight, premature infants. In line with research on the positive effects of human milk on the developing brain, it was expected that infants fed increased quantities of breast milk would show a more mature neurobehavioral profile in the neonatal period and higher cognitive skills in infancy. Neurobehavioral maturation was assessed with the Neonatal Behavior Assessment Scale (NBAS; Brazelton, 1973) with a particular emphasis on the relationship of breast milk and habituation, state, and motor development (Field, 1995; Mayes, Granger, Frank, Schottenfeld, & Bornstein, 1993). As the range of state cluster of the NBAS has been shown to predict visual acuity (Colombo, Moss, & Horowitz, 1989), evaluating infants' functioning on the range of state was of special interest in light of research linking breast milk intake and visual acuity in premature infants (O'Connor et al., 2001). Several studies reported a dose–response pattern in the effects of breast milk on IQ (Mortensen et al., 2002; Quinn et al., 2001), and thus, outcomes were compared for three groups of infants: those receiving substantial (>75% of nutrition), intermediate (25–75%), and minimal (<25%) amounts of breast milk. Infants suffering from conditions that are clearly associated with poor cognitive outcomes, such as congenital malformation or severe hemorrhage, poverty, single parenting, teenage mothering, and maternal drug use, were excluded from the study.

In addition, it was hypothesized that mothers providing more breast milk would be less depressed, would demonstrate more affectionate touch, and their infants would be more alert during social interactions. Consistent with research on the relations between lower maternal depression and more frequent touch with improved cognitive development in premature infants (Feldman et al., 2002), increased maternal touch and lower depression were expected to correlate with better cognitive outcomes. The moderating role of maternal touch was examined according to a model outlined by Baron and Kenny (1986). This moderator model evaluated the role of maternal touch in enhancing the relations between the amount of breast milk ingested in the neonatal period and later cognitive development.

SUBJECTS AND METHODS

Participants

Eighty-six premature infants who were born before 33 weeks GA with a birth weight of below 1750 g were studied. Infants' mean birth weight was 1298 g ($SD = 335.58$, range = 640–1720 g), and mean gestational age was 30.45 weeks ($SD = 3.02$, range = 26–33 weeks). Of these, 34 infants received a substantial amount of maternal milk (>75% of nutrition), 21 received intermediate amounts of maternal milk supplemented by formula (between 25–75% of nutrition), and 31 infants received a minimal amount of maternal milk (<25% of nutrition). Infants were excluded from the study if they had IVH Grades III or IV or suffered from perinatal asphyxia, metabolic, or genetic disease. All mothers in the study were married to the infant's father, parents had at least high-school education, mothers were at least 20 years old, and all families were considered middle class by Israeli standards (Harlap, Davis, Grower, & Prywes, 1977). None of the mothers smoked or used drugs during the pregnancy. No differences were found in infants' birth weight, gestational age (GA), the degree of medical risk, and birth order (first-born/later born) between the three groups. Similarly, maternal and paternal age and education and the level of mothers' self-reported social support (Crockenberg, 1987) was comparable in the three groups. No differences were found in the infants' Apgar 1- and 5-min scores, a measure of the newborn's cardiorespiratory and neurological functioning immediately after birth. All infants received standard nursery care and were not involved in any intervention programs. Infant and family information are summarized in Table 1.

Recruitment

As part of a larg-scale follow-up, consecutive mothers and infants born at the Shaare Zedek Medical Center between March 1996 and April 1999 and matched the study criteria were approached once the infant's medical condition stabilized. Of those approached, six mothers declined participation, and their demographic and infant conditions were similar to the participating families, including the provision of breast milk. The study was approved by the Institutional Review Board, and informed consent was obtained from all participants.

Procedure and Measures

The exact amount of breast milk and formula the infant received (in cc) was registered after each meal by the nursing staff. Hospital policy precludes the use of donor milk, and all breast milk the infant received was the mother's own. All feedings were initially via a nasogastric tube, and all infants received the same formula (Similac, Premature Special Care). Infants remained in the neonatal intensive care unit throughout their entire

Table 1. Family Demographic and Infant Medical Variables

	Substantial Milk ($n = 34$)		Intermediate Milk ($n = 21$)		Minimal Milk ($n = 31$)	
	M	*SD*	*M*	*SD*	*M*	*SD*
Birth weight (g)	1302.25	320.21	1298.51	309.49	1354.11	388.31
GA (weeks) at birth	30.79	2.37	29.86	3.28	31.14	3.54
CRIB (score)	2.29	2.63	2.83	3.56	2.48	3.34
Mother age (yr)	28.63	5.35	29.08	6.14	29.87	5.79
Mother education (yr)	14.73	1.96	13.58	3.12	13.96	1.98
Father age (yr)	30.78	8.13	31.60	5.55	31.94	7.08
Father education (yr)	13.92	3.13	13.40	4.09	13.28	4.76
Gender ratio (M/F)	19/17		12/9		15/17	
First-born/later-born	15/21		9/12		13/19	
Apgar 1 min	7.92	1.88	7.33	2.73	7.87	1.68
Apgar 5 min	8.50	1.46	8.13	1.32	8.62	1.46

Note. GA = gestational age.

hospitalization. For each day, the amounts of formula and breast milk (in cc) were computed, and a total sum was computed for the entire hospitalization period. The following variables were computed: (a) the amount of breast milk (in cc) during the hospitalization period, (b) the amount of formula (in cc) during the hospitalization period, (c) the proportion of breast milk infants received [ratio of a to (b + a)], (d) infant postnatal age (days) at the first breast milk feeding, and (e) infant GA age (weeks) at the first day of breast milk feeding. Infants were fed by gavage (nasogastric tube) until 34 to 35 weeks GA and were then gradually fed increased amounts by bottle. Infants were weaned off gavage feeds by 36 weeks GA. The number of breast-feeding episodes was less than 5% of all feeding episodes for all infants, even for infants receiving a substantial amount of breast milk. To control for breast-feeding, the number of breast-feeding episodes was used as a covariate in the analyses. Infants were assigned to the three groups based on the proportion of breast milk during the entire hospitalization (Variable *c*).

37 Weeks' GA

Infant Medical Risk. Infant medical risk was measured according to the CRIB (International Neonatal Network, 1993). The CRIB is an objective quantitative measure of neonatal risk for infants born prematurely, which scores for birth weight, GA, minimum and maximum fraction of inspired oxygen, minimum base excess during the first 12 hr, and the presence or absence of congenital malformations. Individual scores are summed to create the total CRIB score.

Mother–Infant Interaction

Ten minutes of mother–infant interaction were videotaped and coded. Videotaping took place after the mid-morning feeding, to control for fluctuations in neonates' arousal before and after feeding, and filming started when the infant was in an awake and calm state. Mothers sat in a comfortable chair in a quiet, empty room (including a changing table and a sink) in the NICU, and videotaping was conducted through a screening window. Mothers were asked to interact with the infant freely for 10 min, but no specific instructions were provided. Coding of all tapes was conducted at a central university laboratory by trained observers unaware of the infant's group membership or the study's hypotheses. Coding was conducted using the Mother–Newborn Coding System (Feldman, 1998), which has been validated in studies of mother–newborn interactions (Feldman et al., 2002; Keren, Feldman, Eidelman, Sirota, & Lester, 2003). The coding system consists of four maternal categories and one infant category, and each category includes a set of mutually exclusive codes. For 10-s epoch, the coder selects one option for each category. Two graduate students in psychology coded the videotapes. Training was conducted using a training tape of 15 mother–newborn interactions of full-term and preterm infants who were not part of the present study, and training continued until 85% agreement was achieved in all categories.

Categories, codes included in each category, and reliability for each category were as follows; *Maternal Gaze*: to infant's face, to infant's body, to object, gaze aversion ($\kappa = .84$); *Maternal Affect*: positive, negative, neutral ($\kappa = .79$); *Maternal Talk*: no talk, talk to infant, sing, "motherese" ($\kappa = .85$); *Maternal Touch*: no touch, functional touch (e.g., wipe the infant's mouth), loving touch (mother touching infant with clear positive affect and no functional purpose), hug, cradle, and stimulate ($\kappa = .83$); *Infant State*: fuss, cry, alert-scanning, gaze aversion, and sleep ($\kappa = .80$). Reliability was conducted for 15 mother–infant dyads, and reliability averaged 93% ($\kappa = .82$). The following variables were considered to index the mother's warm and affectionate style as well as the infant's participation in the interaction and were used in the present study. *Maternal Positive Affect*: the proportion of time mothers spent in positive affect (i.e., the proportion of 10-s units mother was in positive affect of the entire 10-min period); *Maternal Affectionate Touch*: sum of the proportions of loving touch, hug, cradle, and stimulate, *Maternal Vocalization*: sum of talk to infant, sing, and vocalize; *Infant Alert*: the proportion of time the infant was in an alert-scanning state was used to index the infant's participation in the interaction.

Maternal Depression

Maternal depression was assessed with the Beck Depression Inventory (BDI; Beck, 1978), a well-validated self-report instrument for the assessment of depression.

Neurodevelopmental Status

One to 2 days prior to discharge, infants were tested with the NBAS (Brazelton, 1973) by a trained neonatologist who was blind to feeding status. All infants were discharged after 36 weeks' GA (37–38 weeks' GA). Items were composited into six clusters (Lester, 1984), and the habituation, motor maturity, and range of states were examined in this study.

6 Months' Corrected Age

Infant cognitive development was assessed by a trained psychologist blind to group assignment, with the *Bayley Scale of Infant Development*, second edition (Bayley, 1993). The Bayley-II yields two developmental indices: the Mental Development Index (MDI) and the Psychomotor Developmental Index (PDI).

RESULTS

Prior to data analysis, descriptive statistics on variables pertaining to clinical and feeding practices and the differences between groups on these variables are presented. These data appear Table 2.

As seen in Table 2, infants in the three groups spent the same number of days in the hospital and received a comparable number of feedings. The amount of breast milk clearly distinguished between groups. In addition to differences in amounts, mothers in the substantial milk group were the quickest to provide milk, and infants in this group were the youngest in terms of both postbirth age and postconceptual age at the first breast milk feeding.

Differences in Mother–Infant Interaction, Neurobehavioral Maturation, and Cognitive Development in Relation to Breast Milk

Mother–Infant Interactions. A multivariate analysis of covariance (MANCOVA) with breast milk group (substantial, intermediate, minimal) and infant gender as the between-subject factors and the number of breast-feeding episodes as the covariate was computed for the four mother–infant interaction variables (maternal affect, affectionate touch, vocalization, and infant alert) at 37 weeks' GA. An overall main effect for breast milk group was found; Wilks' $F(8, 152) = 3.86$, $p < .01$, demonstrating that mother–infant interaction patterns differed according to the amount of ingested breast milk. Univariate tests (Table 3) showed that mothers who gave more milk provided more frequent affectionate touch, talked to their infants less, and their infants were more alert during interactions. Post hoc comparisons indicated that mothers who provided a substantial amount of milk exhibited significantly more affectionate touch than mothers in the intermediate milk group, and mothers in the intermediate group provided significantly more affectionate touch than mothers in the minimal milk group (a dose–response pattern). The reverse pattern was found for talk, with mothers in the minimal milk group talking the most. Infants in the substantial milk group were significantly more alert than infants in the other two groups, but no significant difference was found between the intermediate and minimal groups in infant alertnes (Figure 1). No gender-related effects were found.

Neurobehavioral Maturation. A MANCOVA with breast milk group (substantial, intermediate, minimal) and infant gender as the between-subject factors and the

Table 2. Clinical and Feeding Variables

	Substantial Milk		Intermediate Milk		Minimal Milk		
	M	*SD*	*M*	*SD*	*M*	*SD*	*F*
Days in hospital (*n*)	56.3	29.4	59.3	32.6	54.6	27.5	n.s.
Feedings (*n*)	317.1	118.6	324.6	124.7	307.2	108.3	n.s.
Infant age (days) at first breast milk	4.3	1.7	5.3	2.3	6.7	4.2	3.37*
GA (weeks) at first breast milk	30.6	1.7	31.2	2.8	32.9	2.3	3.12*
Total amount of breast milk (cc)	7375.2	3211.6	3498.8	1160.2	970.2	200.0	34.5**
Total amount of formula (cc)	1404.8	602.7	5708.3	1922.5	7848.1	3668.3	26.4**
Proportion of breast milk	.84	.23	.38	.22	.11	.09	32.5**

Note. GA = gestational age.
*$p < .05$.
**$p < .001$.

Table 3. Group Differences in Mother–Infant Interaction, Neurodevelopment, and Cognitive Development

	Substantial Milk (a)		Intermediate Milk (b)		Minimal Milk (c)		
	M	*SD*	*M*	*SD*	*M*	*SD*	Univariate *F*
Mother–infant interaction							
Maternal affect	16.07	10.58	14.08	11.61	12.64	9.35	1.02
Maternal talk	4.44	4.50	7.22	6.74	9.87	8.49	3.52* (a < b < c)
Maternal affectionate touch	21.51	11.79	17.78	9.03	13.06	9.51	3.68* (a > b > c)
Infant alert	9.51	7.96	4.08	3.82	4.20	4.98	4.42** (a > b, c)
Neurobehavioral maturation (NBAS)							
Habituation	6.41	.96	6.27	1.33	6.39	.84	.65
Motor maturity	4.70	.66	4.48	.67	4.12	.57	3.23* (a > b > c)
Range of state	3.99	.46	3.52	.65	3.55	.63	3.37* (a > b, c)
Cognitive Development							
MDI	94.16	8.75	91.66	7.20	90.53	8.54	3.34* (a > b, c)
PDI	85.75	11.46	78.60	12.57	78.00	11.36	5.21** (a > b, c)

Note. MDI = Mental Development Index; PDI = Psychomotor Development Index; NBAS = Neonatal Behavioral Assessment Scale.
*$p < .05$.
**$p < .01$.

number of breast-feeding episodes as the covariate was computed for the three NBAS clusters (habituation, motor maturity, range of states). An overall main effect for breast milk group was found, Wilks' $F(6, 154) = 2.58$, $p < .05$, and no gender effects. Univariate tests (Table 3) revealed significant group differences in motor maturity and range of states, but not in habituation. Post hoc comparisons showed a dose–response pattern for motor maturity; infants in the substantial breast milk group scored the highest, infants in the intermediate group scored significantly less than infants in the substantial group, and infants in the minimal group showed lower motor maturity compared to infants in the intermediate group. On the range of states cluster, differences were found only between the substantial milk group and the other two groups, and no differences emerged between the intermediate and minimal groups (Figure 2).

Cognitive Development. A similar MANCOVA with breast milk and infant gender as the between-subject factors and the number of breast-feeding episodes as the covariate was computed for the two cognitive indices at 6 months (MDI, PDI). An overall main effect for breast milk group was found, Wilks' $F(4, 156) = 3.14$, $p < .05$. Univariate analyses showed group differences on both

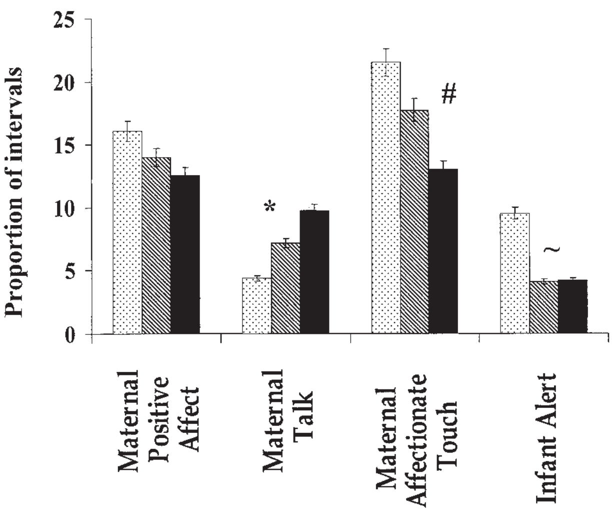

FIGURE 1 Mother–infant interaction patterns at 27 weeks GA among infants receiving substantial (**A**, dotted columns), intermediate (**B**, striped columns), and minimal (**C**, black columns) amounts of breast milk. *For maternal talk, A < B < C; $p < .05$. #For maternal affectionate touch, A > B > C; $p < .05$. ~For infant alert, A > B, C; $p < .01$.

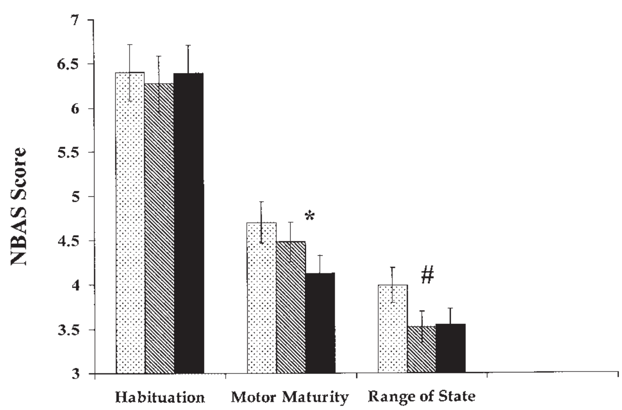

FIGURE 2 Neurobehavioral maturation at 37 weeks GA among infants receiving substantial (**A**, dotted columns), intermediate (**B**, striped columns), and minimal (**C**, black columns) amounts of breast milk. *For motor maturity, A > B > C; $p < .05$. #For range of state, A > B, C; $p < .05$.

the MDI and PDI scores (Table 3). Post hoc comparisons indicated that significant differences in mental and psychomotor development were found only between the substantial-milk group and the other two groups, with no differences between the minimal and intermediate groups. No differences related to infant gender were found (Figure 3).

Associations Between Breast Milk, Maternal Affectionate Touch, Maternal Depression, and Infant Neurodevelopmental and Cognitive Development

Maternal depression was negatively related to the amount of breast milk, $r = -.31$, $p > .01$, and positively related to the latency to the first feeding of breast milk, $r = .33$, $p < .05$. Significant negative correlations also were found between maternal depression and maternal affectionate touch, $r = -.24$, $p < .05$. Significant negative relations were found between maternal depression and infants' MDI scores at 6 months, $r = -.25$, $p < .05$, but not with their PDI scores, $r = -.11$, $p > .10$. Maternal depression was unrelated to neurobehavioral functioning. Maternal affectionate touch was related to higher motor maturity, $r = .27$, $p < .05$, to increased infant alertness during the interaction, $r = .36$, $p < .01$, and to better psychomotor skills at 6 months, $r = .31$, $p < .01$. The range of states cluster was related to MDI scores at 6 months, $r = .26$, $p < .05$.

Predicting Infants' Cognitive Development: A Moderator Model

Two hierarchical regression equations were computed to evaluate the moderating role of maternal affectionate touch (moderator) on the relations between the amount of breast milk (predictor) and cognitive development (criterion). According to Baron and Kenny (1986), a moderator is a variable that functions to enhance or attenuate the relations between the predictor and the criterion, and is implied when the interaction of the predictor and the moderator explains unique variance while controlling for both the predictor and the moderator. Predictors were entered in four blocks in the following order: In the first block, infants' medical risk was indexed by the CRIB score to partial out variance due to biological risk; in the second, the amount of breast milk was entered; in the third, maternal affectionate touch was entered; and in the final block, the interaction of maternal milk and maternal affectionate touch was entered. Results of the two models are presented in Table 4.

Results reported in Table 4 indicate that infant medical risk was a meaningful predictor of both MDI and PDI scores, indicating poorer mental and motor outcomes among more medically compromised infants. The amount of breast milk was a unique predictor in both models, confirming to the independent effects of breast milk on the mental and motor development of preterm infants. Maternal affectionate touch uniquely predicted PDI, but not MDI scores. However, a moderator model was found only for MDI, as indicated by the findings that the interaction of breast milk and maternal affectionate touch explained unique variance while both breast milk and maternal affectionate touch were controlled. These findings may suggest that in the motor domain there are two independent effects on development; one of breast milk and the other of increased maternal affectionate touch. On the other hand, in the mental domain, maternal affectionate touch does not have an independent effect but functions to enhance the impact of breast milk on the infant's cognitive growth. To explore the interaction, maternal affectionate touch was divided at the median to high- and low-touch groups. Comparison of the means show that premature infants who received a substantial amount of maternal milk *and* high levels of maternal affectionate touch showed the highest MDI scores ($M = 95.71$, $SD = 6.75$) compared to all other groups ($M = 90.30$, $SD = 7.17$).

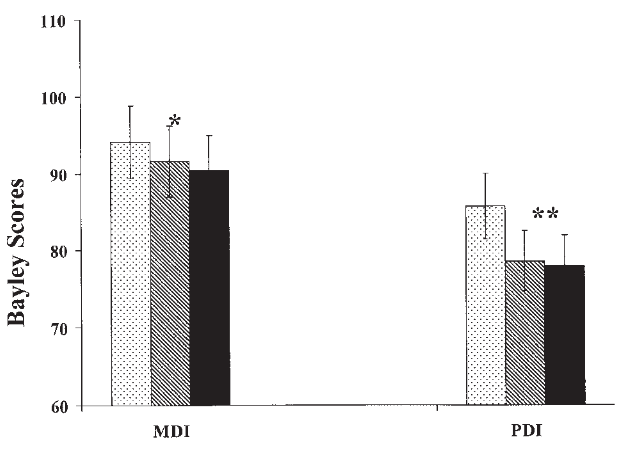

FIGURE 3 Mental (MDI) and psychomotor (PDI) development at 6 months corrected age in infants receiving substantial (**A**, dotted columns), intermediate (**B**, striped columns), and minimal (**C**, black columns) amounts of breast milk. *For MDI, A > B, C; $p < .05$. **For PDI, A > B, C; $p < .01$.

DISCUSSION

Results of this study indicate that the amount of breast milk ingested in the neonatal period is related to neurological and cognitive development in low-birth-weight, premature infants. Differences among groups were significant although the groups were comparable on a wide range of socio-demographic and medical factors, suggesting that the outcomes are not solely related to environ-

Table 4. Examining the Moderating Role of Maternal Touch on the Relations of Maternal Milk and Infants' Cognitive Development

	Mental Developmental Index			Psychomotor Developmental Index		
Criterion	Beta	R^2 Change	F Change	Beta	R^2 Change	F Change
Medical risk (CRIB)	−.28*	.07	5.04*	−.27*	.06	3.96*
Proportion of breast milk	.40*	.06	3.99**	.45**	.06	4.55*
Maternal affectionate touch	.32	.02	1.93	.40*	.05	3.85*
Breast milk* maternal affectionate touch	−.48**	.06	4.25*	−.41	.02	1.87
	R^2 Total = .21; $F(4, 83) = 3.98$, $p < .01$			R^2 Total = .19; $F(4, 83) = 3.73$, $p < .01$		

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

mental conditions. Infants who received a substantial amount of breast milk (>75% of nutrition) showed a more mature neurodevelopmental profile at 37 weeks' GA and higher mental and psychomotor skills at 6 months' corrected age. In addition, breast milk was associated with more optimal maternal–infant interactive patterns, in terms of increased maternal affectionate touch and greater infant alertness during interactions, and with lower maternal depression. Consistent with the two mechanisms proposed to underlie the relations of breast milk and development (Quinn et al., 2001), a direct relationship was found between breast milk and cognitive skills as well as associations between breast milk and more optimal maternal mood and interaction patterns, which in turn correlated with improved cognitive outcomes.

The associations found between breast milk and cognitive development in premature infants is consistent with previous research (Bier et al., 2002; Horwood et al., 2001; Lucas et al., 1992). The nutritional content of breast milk is of particular importance to the vulnerable premature infant, and supplementing preterm formula with long-chain polyunsaturated fatty acids has been shown to improve visual acuity and cognitive maturation (O'Connor et al., 2001). The results indicated that higher cognitive scores were found only for the group receiving a substantial amount of breast milk, suggesting that there is a critical amount of breast milk and its unique constituents that must be supplied to make a lasting impact on the development of high-risk infants.

Evaluating infants with the NBAS afforded us the opportunity to measure neurobehavioral performance as related to breast milk. Ingestion of breast milk was related to maturation of state and motor function. The range of state cluster addresses the infant's capacity to use the entire spectrum of states and move flexibly between states to adapt to internal and external cues. Intact state organization provides the basis for attentional and cognitive processes (Dahl, 1996) and predicts visual processing (Feldman & Mayes, 1999), cognitive development (Thoman, Denenberg, Sievel, Zeidner, & Becker, 1981), emotion regulation, and exploratory behavior (Feldman, Weller, Sirota, & Eidelman, 2002). Our findings similarly showed a correlation between better range of state in the neonatal period and higher cognitive skills. As breast milk was found here to be associated with better state organization in premature infants, it may have improved the infant's attention and arousal regulation, leading to improved cognitive development. Interestingly, on both the range of states and the MDI, only infants in the substantial milk group showed higher scores, which confirms the need for a critical amount of breast milk for more optimal development in this neurodevelopmental process.

Motor maturity was related to the amount of breast milk and to frequent maternal affectionate touch, pointing to the links between motor development, touch, and feeding. Touch therapy applied to preterm infants in the hospitalization period was found to improve motor maturity (Field, 1995) and to increase weight gain per caloric intake (Goldstein-Ferber et al., 2002). It is possible that in addition to the contribution of breast milk to growth, pumping milk also facilitates more maternal affectionate touch. Touch, in turn, may contribute to the infant's growth and development (Field, 1995; Tronick, 1996). Interestingly, both maternal affectionate touch and motor maturity showed a dose–response pattern, which may suggest that—unlike the range of states and MDI—differential amounts of breast milk differently affect the development of both maternal affectionate touch patterns and motor neurofunctions in a dose–response effect.

In addition to the links between breast milk and infants' neurobehavioral and cognitive development, providing milk was related to better maternal mood and interactive behavior. Maternal depression was related to lower quantities of breast milk and to longer latencies to the first breast-feeding. It is possible that the timing of the first provision of breast milk plays a role in the relations of breast milk and maternal depression, as seen by the findings that mothers who were quicker to provide breast milk reported less depressive symptoms. Maternal depression also was related to reduced maternal affectionate touch and lower infant cognitive skills. These findings are in line with extant research on the negative impact of maternal depression on children's cognitive and social development (Goodman & Gotlieb, 1999).

Research in animals has pointed to the role of oxytocin and prolactin in the initiation of maternal behavior, such as affiliative touch, grooming, and proximity seeking (Grattan et al., 2001; Insel, 1997; Nelson & Panksepp, 1998). In humans, studies have implicated oxytocin in the regulation of stress and negative mood in lactating mothers (Carter & Altemus, 1997). Little research, however, has integrated the components of the social bonding system with findings on maternal negative mood in a human model. The present findings may offer a first step by pointing to associations between the amount of maternal breast milk, the frequency of maternal affectionate touch—a special form of parental touch that differs from touch of non-kin caregivers (Miller & Holditch-Davis, 1992)—and the level of maternal depression. Although oxytocin levels were not examined here, the link between breast pumping and increase in oxytocin has been documented (Yokoyama et al., 1994; Zinaman et al., 1992). The present findings may suggest that providing breast milk functions to initiate a more optimal bonding process between mothers and their premature infants by operating on physiological, behavioral, and representational (e.g., mood) systems.

Finally, the amount of breast milk correlated with maternal affectionate touch during interactions. Associations between lactation and increased maternal grooming and proximity-seeking behaviors have been reported in other mammals, and possibly apply to the human mother in the postbirth period (Insel, 1997). It has been suggested that maternal affectionate touch serves an essential regulatory function to the infant's internal systems, and its role is particularly central in the immediate postbirth period—a time when touch should comprise the bulk of the newborn's sensory experiences (Tronick, 1996). Increased maternal affectionate touch also has been shown to predict the mother's readiness for the maternal role following premature birth (Keren et al., 2003), pointing to the associations between maternal affectionate touch and the mother's internal state. The results also indicate that maternal affectionate touch correlated with infants' visual alertness during interactions, suggesting that touch plays a role in the mother–infant earliest social relationship. Results of the moderator model indicate that maternal affectionate touch functions to enhance the relations between breast milk and cognitive skills. One possibility is that providing breast milk is related to more maternal affectionate touch, which in turn supports cognitive growth among premature infants whose growth trajectory has already been improved by the nutritional content of human milk. This hypothesis, however, is preliminary and requires much further testing. Evidence points to a close interaction between biological and environmental conditions in shaping developmental outcomes among high-risk preterms (Bendersky & Lewis, 1994; Weisglas-Kuperus, Baerts, Smrkovsky, & Sauer, 1993). The present findings may similarly suggest an integration of the nutritional aspects of breast milk with the maternal relational and behavioral aspects of providing breast milk in promoting neurological and cognitive growth among low-birth-weight, preterm infants.

The link between breast milk and infant development is a complex issue that requires much further research. In addition to existing research on cognitive development, we need to know whether breast milk contributes to children's social, emotional, and self-regulatory skills. For theoretical and practical reasons, it is important to study the domains in which mothers' and donors' milk exert comparable effects on the development of premature infants, and the domains where mother's own milk carries a special impact on the mother–child relationship and on the mothering process. Finally, future research should delineate the amount, duration, and age of onset of breast milk nutrition that is most beneficial for the physical, cognitive, and social–emotional growth of these vulnerable, premature infants.

NOTES

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REFERENCES

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology, 51, 1173–1182.

Bayley, N. (1993). Bayley Scales of Infant Development: Administering and scoring manual. New York: Psychological Corporation.

Beck, A. T. (1978). Beck Depression Inventory. The Psychological Corporation, San Antonio, TX: Harcourt Brace Jovanovich.

Bendersky, M., & Lewis, M. (1994). Environmental risk, biological risk, and developmental outcome. Developmental Psychology, 30, 484–495.

Bier, J. A., Oliver, T., Ferguson, A. E., & Vohr, B. R. (2002). Human milk improves cognitive and motor development of premature infants during infancy. Journal of Human Lactation, 18, 361–367.

Boersma, E. R., & Lanting, C. I. (2000). Environmental exposure to polychlorinated biphenyls (PCBs) and dioxins: Consequences for long-term neurological and cognitive development of the child lactation. Advances in Experimental Medicine and Biology, 478, 271–287.

Brandt, K. A., Andrews, C. B., & Kvale, J. (1998). Mother–infant interaction and breast-feeding outcomes 6 weeks after birth. Journal of Obstetric, Gynecologic, and Neonatal Nursing, 27, 169–174.

Brazelton, T. B. (1973). The Neonatal Behavioral Assessment Scale. Philadelphia: Lippincott.

Brooten, D., Gennaro, S., Brown, L., Butts, P., Gibbons, A., & Bakewill-Sachs, S. (1988). Anxiety, depression, and hostility in mothers of preterm infants. Nursing Research, 37, 213–216.

Carter, C. S. (1998). Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology, 23, 779–818.

Carter, C. S., & Altemus, M. (1997). Integrative functions of lactational hormones in social behavior and stress management. Annals of the New York Academy of Sciences, 807, 164–174.

Colombo, J., Moss, M., & Horowitz, F. D. (1989). Neonatal state profiles: Reliability and short-term prediction of neurobehavioral status. Child Development, 60, 1102–1110.

Crockenberg, S. (1987). Predictors and correlates of anger toward and punitive control of toddlers by adolescent mothers. Child Development, 58, 964–975.

Dahl, R. E. (1996). The regulation of sleep and arousal: Development and psychopathology. Development and Psychopathology, 8, 3–27.

Davis, D. H., & Thoman, E. B. (1988). The early social environment of premature and full-term infants. Early Human Development, 17, 221–232.

Eckerman, C. O., Hsu, H. C., Molitor, A., Leung, E. H., & Goldstein, R. F. (1999). Infant arousal in an en-face exchange with a new partner: Effects of prematurity and perinatal biological risk. Developmental Psychology, 35, 282–293.

Feist, N., Berger, D., & Speer, C. P. (2000). Anti-endotoxin antibodies in human milk: Correlation with infection of the newborn. Acta Paediatrica, 89, 1087–1092.

Feldman, R. (1998). Mother–Newborn Coding System Manual. Bar-Ilan University .

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., & Mayes, L. C. (1999). The rhythmic organization of infant attention during habituation is related to infants' information processing. Infant Behavior and Development, 22, 37–49.

Feldman, R., Weller, A., Leckman, J. F., Kvint, J., & Eidelman, A. I. (1999). The nature of the mother's tie to her infant: Maternal bonding under conditions of proximity, separation, and potential loss. Journal of Child Psychology and Psychiatry, 40, 929–940.

Feldman, R., Weller, A., Sirota, I., & 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.

Field, T. (1995). Massage therapy for infants and children. Journal of Behavioral and Developmental Pediatrics, 16, 105–111.

Furman, L., Minich, N. M., & Hack, M. (1998). Breast-feeding of very low birth weight infants. Journal of Human Lactation, 14, 29–34.

Gale, C. R., & Martyn, C. N. (1996). Breast-feeding, dummy use, and adult intelligence. Lancet, 347, 1072–1075.

Golding, J., Rogers, I. S., & Emmett, P. M. (1997). Association between breast-feeding, child development, and behavior. Early Human Development, 49(Suppl.), S175–S184.

Goldstein-Ferber, S., Kuint, J., Weller, A., Dolberg, S., Feldman, R., Arbel, E., & Kohelet, D. (2002). Massage therapy by mothers and trained professionals enhances weight gain in preterm infants. Early Human Development, 67, 37–45.

Goodman, S. H., & Gotlieb, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. Psychological Review, 106, 458–490.

Grattan, D. R., Pi, X. J., Andrews, Z. B., Augustine, R. A., Kokay, I. C., Summerfield, M. R., Todd, B., & Bunn, S. J. (2001). Prolactin receptors in the brain during pregnancy and lactation: Implications for behavior. Hormones and Behavior, 40, 115–124.

Greene, J. G., Fox, N. A., & Lewis, M. (1983). The relationship between neonatal characteristics and three-month mother–infant interaction in high-risk infants. Child Development, 54, 1286–1296.

Harlap, S., Davis, A. M., Grower, M. B., & Prywes, B. (1977). The Jerusalem perinatal study: The first decade (1964–1977). Israel Medical Journal, 13, 1073–1091.

Heird, W. C. (2001). The role of polyunsaturated fatty acids in term and preterm infants and breast-feeding mothers. Pediatric Clinics of North America, 48, 173–188.

Horwood, L. J., Darlow, B. A., & Mogridge, N. (2001). Breast milk feeding and cognitive ability at 7 to 8 years. Archives of Diseases in Childhood Fetal and Neonatal Edition, 84, F23–F27.

Insel, T. R. (1992). Oxytocin—A neuropeptide for affiliation: Evidence from behavioral, receptor, autoradiographic, and comparative studies. Psychoneuroendocrinology, 17, 3–35.

Insel, T. R. (1997). A neurobiological basis of social attachment. American Journal of Psychiatry, 154, 726–735.

International Neonatal Network. (1993). The CRIB (clinical risk index for babies) score: A tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. Lancet, 342, 193–198.

Jacobson, S. W., Chiodo, L. M., & Jacobson, J. L. (1999). Breast-feeding effects on intelligence quotient in 4- and 11-year-old children. Pediatrics, 103, e71.

Jain, A., Concato, J., & Leventhal, J. M. (2002). How good is the evidence linking breast-feeding and intelligence? Pediatrics, 109, 1044–1053.

Johnson, D. L., Swank, P. R., Howie, V. M., Baldwin, C. D., & Owen, M. (1996). Breast-feeding and children's intelligence, Psychological Reports, 79, 1179–1185.

Keren, M., Feldman, R., Eidelman, A. I. Sirota, L., & Lester, B. (2003). Clinical interview for high-risk parents of premature infants (CLIP): Relations to mother–infant interaction. Infant Mental Health Journal, 24, 93–110.

Killersreiter, B., Grimmer, I., Buhrer, C., Dudenhausen, J. W., & Oblade, M. (2002). Early cessation of breast milk feeding in very low birth weight infants. Early Human Development, 60, 193–205.

Koletzko, B., Rodriguez-Palmero, M., Demmelmair, H., Fidler, N., Jensen, R., & Sauerwald, T. (2001). Physiological aspects of human milk lipids. Early Human Development, 65, S3–S18.

Larque, E., Demmelmair, H., & Koletzko, B. (2002). Perinatal supply and metabolism of long-chain polyunsaturated fatty acids. Annals of the New York Academy of Sciences, 967, 299–310.

Lester, B. M. (1984). Data analysis and prediction. In T. B. Brazelton (Ed.), Neonatal Behavioral Assessment Scale (2nd ed.) London: Spastic International Medical Publications.

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.

Lucas, A., Cole, T. J., Morley, R., Lucas, P. J., Davis, J. A., Bamford, M. F., Crowle, P., Dossetor, J. F., Pearse, R., & Boon, A. (1998). Factors associated with maternal choice to provide breast milk for low-birth-weight infants. Archives of Diseases in Childhood, 63, 48–52.

Lucas, A., Morley, R., Cole, T. J., Lister, G., & Leeson-Payne, C. (1992). Breast milk and subsequent intelligence quotient in children born preterm. Lancet, 339, 261–264.

Malatesta, C. Z., Grigoryev, P., Lamb, C., Albin, M., & Culver, C. (1986). Emotion socialization and expressive development in preterm and full-term infants. Child Development, 57, 316–330.

Matthiesen, A. S., Ransjo-Arvidson, A. B., Nissen, E., & Uvnas-Moberg, K. (2001). Postpartum maternal oxytocin release by newborns: Effects of infant hand massage and sucking. Birth, 28, 13–19.

Mayes, L. C., Granger, R. H., Frank, M. A., Schottenfeld, R., & Bornstein, M. H. (1993). Neurobehavioral profiles of neonates exposed to cocaine prenatally. Pediatrics, 91, 778–783.

Miller, D. B., & Holditch-Davis, D. (1992). Interactions of parents and nurses with high-risk preterm infants. Research in Nursing and Health, 15, 187–197.

Minde, K. (2000). Prematurity and serious medical conditions in infancy: Implications for development, behavior, and intervention. In C. H. Zeanah (Ed.), Handbook of infant mental health (pp. 176–194). New York: Guilford Press.

Mortensen, E. L., Michaelsen, K. F., Sanders, S. A., & Reinisch, J. M. (2002). The association between duration of breast-feeding and adult intelligence. JAMA, 287, 2365–2371.

Nelson, E. E., & Panksepp, J. (1998). Brain substrates of infant–mother attachment: Contributions of opioids, oxytocin, and norepinephrine. Neuroscience and Biobehavioral Reviews, 22, 437–452.

Newton, N. (1992). The quantitative effect of oxytocin (pitocin) on human milk yield. Annals of the New York Academy of Sciences, 652, 481–483.

Nissen, E., Lilja, G., Widstrom, A. J., & Uvnas-Moberg, K. (1995). Elevation of oxytocin levels early postpartum in woman. Acta Obstetricia et Gynecologica Scandinavica, 74, 530–533.

O'Connor, D. L., Hall, R., Adamkins, D., Auestad, N., Castillo, M., Connor, W. E., Connor, S. L., Fitzgerald, K., Groh-Wargo, S., Hartmann, E. E., Jacobs, J., Janowsky, J., Lucas, A., Margeson, D., Mena, P., Neuringer, M., Nesin, M., Singer, L., Stephenson, T., Szabo, J., & Zemon, V. (2001). Growth and development in preterm infants fed long-chain polyunsaturated fatty acids: A prospective randomized controlled trial. Pediatrics, 108, 359–371.

Orzalesi, M. (1987). Vitamins and the premature infant. Biology of the Neonate, 52(Suppl.), 97–112.

Quinn, P. J., O'Callaghan, M., Wiliams, G. M., Marjman, J. M., Andersen, M. J., & Bor, W. (2001). The effect of breast-feeding on child development at 5 years: A cohort study. Journal of Pediatrics and Child Health, 37, 465–469.

Richards, M., Wadsworth, M., Rahimi-Foroushani, A., Hardy, R., Kuh, D., & Paul, A. (1998). Infant nutrition and cognitive development in the first offspring of a national U.K. birth cohort. Developmental Medicine and Child Neurology, 40, 163–167.

Schanler, R. J., Hurst, N. M., & Lau, C. (1999). The use of human milk and breast-feeding in premature infants. Clinics in Perinatology, 26, 379–398.

Thoman, E. B., Denenberg, V. H., Sievel, J., Zeidner, L. P., & Becker, P. (1981). State organization in neonates: Developmental inconsistency indicates risk for developmental dysfunction. Neuropediatrics, 12, 45–54.

Tronick, E. Z. (1996). Touch in mother–infant interaction. In T. M. Field (Ed.), Touch in early development (pp. 53–65). Mahwah, NJ: Erlbaum.

Uvnas-Moberg, K. (1998). Oxytocin may mediate the benefits of positive social interaction and emotions. Psychoneuroendocrinology, 23, 819–835.

Weisglas-Kuperus, N., Baerts, W., Smrkovsky, M., & Sauer, P. J. (1993). Effects of biological and social factors on the cognitive development of very low birth weight children. Pediatrics, 92, 658–663.

Yokoyama, Y., Ueda, T., Irahara, M., & Aono, T. (1994). Releases of oxytocin and prolactin during breast massage and suckling in puerperal women. European Journal of Obstetrics, Gynecology, and Reproductive Biology, 53, 17–20.

Zinaman, M. J., Hughes, V., Queenan, J. T., Labobok, M. H., & Albertson, B. (1992). Acute prolactin and oxytocin responses and milk yields to infant suckling and artificial methods of expression in lactating women. Pediatrics, 89, 437–440.