UC Irvine
UC Irvine Previously Published Works

Title

Postnatal maternal cortisol levels predict temperament in healthy breastfed infants

Permalink

Journal

ISSN

Authors

Glynn, Laura M
Davis, Elysia Poggi
Schetter, Christine Dunkel
et al.

Publication Date

DOI

Copyright Information

Peer reviewed

Postnatal maternal cortisol levels predict temperament in healthy breastfed infants

Laura M. Glynn [a],*, Elysia Poggi Davis [a], Christine Dunkel Schetter [b], Aleksandra Chicz-DeMet [a], Calvin J. Hobel [c], Curt A. Sandman [a]

[a] Department of Psychiatry and Human Behavior, University of California, Irvine, United States
[b] Department of Psychology, University of California, Los Angeles, United States
[c] Maternal and Fetal Medicine, Cedars-Sinai Hospital, Los Angeles, United States

Abstract

Background: The implications of the biologically active elements in breast milk for the breastfed infant are largely unknown. Animal models suggest that ingestion of glucocorticoids during the neonatal period influences fear behavior and modifies brain development.
Aims: To determine the association between postnatal maternal cortisol levels and temperament in breastfed infants.
Study design: The relation between maternal cortisol and infant temperament was examined in breastfed and formula-fed infants. Plasma cortisol was used as a surrogate measure for breast milk cortisol levels (plasma and milk levels are correlated in the 0.6 to 0.7 range; [Patacchioli FR, Cigliana G, Cilumbriello A, Perrone G, Capri O, Alemà GS, et al. Maternal plasma and milk free cortisol during the first 3 days of breast-feeding following spontaneous delivery or elective cesarean section. Gynecologic and Obstetric Investigations 1992;34:159-163.]. If exposure to elevated cortisol levels during infancy influences temperament, then a relation between the two should be found among the breastfed infants, but not among the formula-fed infants.
Subjects: Two hundred fifty-three two-month-old infants and their mothers.
Outcome measures: Fearful temperament assessed with the Infant Behavior Questionnaire [Garstein MR, Rothbart MK. Studying infant temperament via the revised infant behavior questionnaire. Infant Behavior and Development 2003;26:64-86].
Results: Among the breastfed infants, higher maternal cortisol levels were associated with reports of increased infant fear behavior (partial $r=0.2$; $p<0.01$). This relation did not exist among the formula-fed infants. Negative maternal affect at the time of assessment did not account for the positive association in the breastfed group.
Conclusions: The findings are consistent with our proposal that exposure to cortisol in breast milk influences infant temperament. Biologically active components in breast milk may represent one avenue through which the mother shapes the development of the human infant during the postnatal period.

* Corresponding author. Department of Psychiatry and Human Behavior, University of California, Irvine, 333 The City Blvd. W., Suite 1200, Orange, CA 92868, United States. Tel.: +1 714 940 1925; fax: +1 714 940 1939.
  E-mail address: lglynn@uci.edu (L.M. Glynn).

1. Introduction

During the prenatal period, the large majority of environmental information the fetus receives is conveyed through biological signals from the maternal environment. In the early postnatal period, the infant is more capable of gathering information on its own, but input from the mother continues to play a critical role in determining its developmental trajectory [3–9]. One avenue through which the mother may exert biological influences on infant development during the postnatal period is through breast milk. For example, it is recognized that breast milk provides nutrition and immune protection for the infant [10]. It is somewhat less well recognized that the components of breast milk also may serve as a means of biochemical communication between mother and offspring [11–13]. Breast milk contains a wide variety of biologically active hormones — including glucocorticoids (GCs; [14,15]), hormones thought to be critical influences on development [16,17].

GCs are stress-sensitive steroid hormones that comprise the endpoint of the hypothalamic–pituitary–adrenal axis. GCs play an essential role in the normal development of the central nervous system [17]. They easily pass the blood brain barrier [18] and the limbic regions, such as the amygdala, involved in the regulation of fear, anxiety and behavioral inhibition, are particularly sensitive to their effects [19,20]. Animals exposed to increased levels of GCs early in life display increased fear and greater behavioral inhibition in the face of novelty [21–24].

A series of studies utilizing a rat model have demonstrated quite convincingly that GCs delivered via milk have lasting influences on the brain and behavior of the exposed offspring. Corticosterone (the primary GC in rodents) levels in milk were manipulated by adding the hormone to the drinking water of dams, which initiated a series of critical events. First, it produced increased levels of corticosterone in the milk and plasma of the treated mothers — levels similar to what would be expected under conditions of mild stress [25]. Second, the labeled corticosterone was found both in the plasma and brain of the pups nursed by the exposed dams [25]. Importantly, the administration of the corticosterone to the dams did not appear to influence maternal behavior [26]. The investigators then determined the short and long-term effects of GC exposure through milk. The adrenal weights of the offspring were slightly but only temporarily reduced (by 30 days there were no differences between the groups; [26,27]). There were reduced physiological (corticosterone) and behavioral (fear) stress responses present at 15 months of age in the GC-exposed group [26–29]. In addition, learning and memory were improved in the animals exposed as infants to GCs and these effects were detectable from weaning through adulthood [26–28]. Last, the animals nursed by the exposed mothers displayed higher numbers of hippocampal GC receptors at both 30 days and at maturity [28,29].

To our knowledge, only one study has considered the relation between GC levels in breast milk and human infant development. Hart et al. [30] examined this relationship in seven to eleven-day-old breastfed infants. The Neonatal Behavioral Assessment Scale was used to assess newborn neuro-behavioral functioning. Infants ingesting higher levels of cortisol (the primary GC in humans) in breast milk scored higher on the Autonomic Stability cluster of the exam, suggesting that cortisol in breast milk was positively associated with the infants ability to regulate their autonomic state and control involuntary responses such as tremors.

The purpose of the present study was to evaluate whether it is plausible that postnatal exposure to GCs in human breast milk influences fearful temperament in infants. As noted
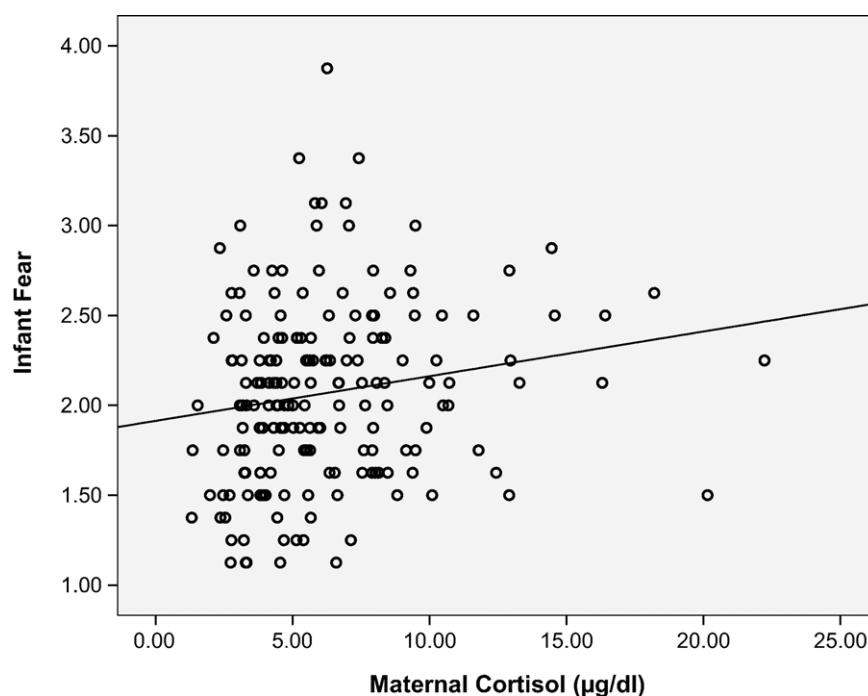

Figure 1   Relation between maternal cortisol and infant fear behavior in breastfed infants ($n = 181$).

above, the limbic regions of the brain which are involved in the regulation of fear, anxiety and behavioral inhibition, represent a primary target for GC exposure [19,20]. If GC exposure via breast milk influences fearful temperament, then we expect to find a relation between maternal cortisol and fearful temperament among breastfed infants, but not among formula-fed infants.

2. Methods

2.1. Participants

Two-hundred fifty-three mother and infant pairs who had been enrolled in a larger longitudinal study of pregnancy at the University of California, Irvine and Cedars-Sinai Medical Center, Los Angeles, participated when the infants were two-months-old (mean = 8.03 weeks; sd = 2.17). The study procedures were approved by the Institutional Review Boards of the participating institutions and all participants provided written informed consent. The initial prenatal enrollment criteria for the longitudinal study were: a) Over 18 years of age b) Singleton intrauterine pregnancy c) English speaking d) Absence of any condition which could affect neuroendocrine function such as endocrine, hepatic or renal disorder or the use of corticosteroid medications, e) Normal uterus and cervix and f) No nicotine, alcohol or drug use. Further, for the current study, those infants who had been admitted to the Neonatal Intensive Care Unit following delivery and those whose mothers were taking corticosteriod medications during the postpartum period were excluded. Of this final sample, 72% of the infants were being breastfed and 28% were formula-fed. Characteristics of the two groups are presented in Table 1.

2.2. Infant temperament

Infant temperament was assessed with an 8-item version of the fear subscale of the Infant Behavior Questionnaire, a widely used parent-report measure of infant temperament [2]. The fear scale assesses the extent to which infants display startle or distress in response to novel or surprising stimuli. Items include questions such as "How often during the past week did the baby startle to a loud sound or sudden noise?". Answers are given on a four-point Likert scale with the endpoints "never" to "always". The Infant Behavior Questionnaire has strong psychometric properties with a Cronbach Alpha coefficient in the current sample of 0.90. Scores on the fear subscale are stable from 2 months to 1 year [31]. Furthermore, the correlation between ratings by the primary and secondary caregiver is 0.75 [2] and maternal report of fearful temperament is correlated with observational measures of infant fear in the laboratory [32,33].

2.3. Plasma cortisol

During the afternoon (mean draw time = 14:01, sd = 1:38) blood samples (20 ml/draw) were obtained by antecubital venipuncture in EDTA (purple top) vacutainers and chilled on ice immediately. The time of day for the blood draw was constrained to control for the diurnal variation in cortisol. Further, an afternoon draw time was selected (as opposed to

Table 1 Sample characteristics

	Breastfed (n = 181)	Formula-fed (n = 72)	t or χ^2
Ethnicity			10.5[*]
Hispanic White	16%	25%	
Non-Hispanic White	56%	37%	
African-American	10%	17%	
Asian	13%	11%	
Other	5%	10%	
Maternal age (years)	31.9 (5.1)	28.6 (5.5)	4.3[*]
Education (% > HS degree)	93%	72%	19.2[*]
Annual household income	$70,099 (31,427)	$50,522 (29,690)	4.4[*]
Marital status (% married)	80%	63%	8.2[*]
Employment (% currently working)	16%	18%	0.2
Sex of infant (% male)	54%	51%	0.2
Birth order (% first born)	59%	56%	0.2
5-minute Apgar score	8.98 (0.22)	8.99 (0.21)	0.8
Birth weight (grams)	3503 (519)	3420 (535)	1.1
Gestational age at birth (weeks)	39.2 (1.46)	39.0 (1.40)	0.9
Infant age at assessment (weeks)	8.2 (2.2)	7.7 (2.1)	1.5
Maternal cortisol (μg/dl)	6.2 (3.43)	6.4 (4.82)	0.23
Fearful temperament[a]	2.1 (0.50)	2.1 (0.51)	0.1

Standard deviations presented in parenthesis when appropriate.

[a] Fearful temperament was assessed with the fear subscale of the Infant Behavior Questionnaire [2]. This four-point Likert scale assesses the extent to which infants display startle or distress in response to novel or surprising stimuli.

[*] $p < 0.05$.

morning) because cortisol levels are more stable at this time of day being less subject to the influences of the time of awakening [34,35]. Samples were centrifuged at 2000 ×g (15 min) and the plasma was decanted into polypropylene tubes containing 500 KIU/ml aprotinin (Sigma Chemical Co.; St. Louis, MO) and stored at −70 °C until assayed.

Plasma cortisol levels were determined by a competitive antibody-coated tube radioimmunoassay (RIA; American Laboratory Products Company, Windham, NH). Plasma samples (25 ul) and ^{125}I-labeled cortisol (500 ul) were added to the antibody-coated tubes and incubated for 45 min in a 37 °C water bath. The aspirated antibody-bound ^{125}I- radiolabeled tubes were quantified with the gamma counter. The assay has <5% cross-reactivity with 11-deoxycortisol, cortisone, prednisone, and <1% cross-reactivity with eight other naturally occurring steroids. The inter- and intra-assay CVs are less than 12% with a minimum detectable level (95% confidence) of 0.22 μg/dL.

Plasma cortisol was used as a surrogate measure for cortisol exposure in breast milk. The relation between circulating cortisol and cortisol in breast milk has been shown to be in the 0.6 to 0.7 range in women on postpartum

day 3 [1]. Although there is no published study in humans demonstrating the strength of the correlation between circulating and breast milk cortisol at any later point during the postnatal period, we believe it is likely that this relation exists beyond 3-days postpartum for the following reasons: 1) Cortisol in breast milk is of adrenal origin. There is no evidence to suggest mammary synthesis [14]. 2) Cortisol in breast milk is present and the levels are similar from 1 to 12 months postpartum [36,37]. 3) The well-documented diurnal variation in plasma cortisol is present in breast milk cortisol from the first through sixth postnatal months [36]. 4) Manipulations of plasma cortisol levels such as administration of dexamethasone, which suppresses plasma cortisol, is associated with a reduction in breast milk cortisol and has been demonstrated across the first 6 months postpartum [36]. 5) Manipulations that result in increases in circulating GCs produce concomitant changes in milk GC levels in non-human animals at various stages of lactation [25,38,39].

2.4. Additional measures

Maternal reports of ethnicity, income, educational level, marital and employment status also were collected. Information about the infants' peri- and neonatal health and Apgar scores was abstracted from the infant's medical record.

At the time of the cortisol collection, the mothers also completed Cohen's Perceived Stress Scale [40], Spielberger's State Anxiety Scale [41,42] and the Center for Epidemiological Studies Depression Scale [43]. These measures of postnatal maternal affect were included to help rule out the possibility that any association seen between cortisol and infant temperament was due to bias related to maternal dysphoria [44]. That is, to assess possibility that mothers who report more anxiety, stress or depression also report more fear behavior in their infants, and that this link might explain any relation between maternal cortisol and infant temperament.

2.5. Data reduction and analysis

The primary outcome variable under examination in the larger longitudinal study from which the current study sample was drawn was preterm birth, not infant temperament. As such, no a priori sample size calculations were conducted for the detection of the associations between maternal cortisol and infant temperament. Data reduction for the RIA assay was accomplished with a computer assisted, four-parameter logistics program [45]. Group differences (breastfed vs. formula-fed) in demographic and infant characteristics first were assessed. The continuous variables were assessed with t-tests and for categorical variables chi-squares were employed. The relation between maternal cortisol levels and infant temperament then were assessed within each group with partial correlations adjusting for infant age at time of assessment. Because of the discrepant sample sizes in two study groups, the differences between correlation coefficients were then tested with the null hypothesis test as recommended by Cohen, et al. [46]. Last, a hierarchical regression analysis was used to assess whether maternal cortisol levels predicted variance above and beyond reports of maternal postpartum affect (depression, anxiety and perceived stress). In this regression model maternal affect, age of infant at assessment and any maternal demographic characteristics such as race/ethnicity, maternal age or parity, that showed a relation at a significance level of less than 0.1 with infant fear were entered first and then maternal cortisol levels were entered second.

3. Results

3.1. Demographic and infant variables among breastfeeding and non-breastfeeding groups

Not surprisingly, the women who were breastfeeding differed from those who were not in that they were more likely to be non-Hispanic White and married, older, more educated and had higher incomes (See Table 1). These relations between breastfeeding status and sociodemographic factors are consistent with those documented previously [47,48].

The two groups did not differ with respect to the infant variables: birth weight, gestational age at birth, 5-minute Apgar scores, birth order, ratio of males to females, or age of infant at assessment (See Table 1). Also, the groups did not differ either in the main predictor variable or in the dependent variable (See Table 1). The groups were similar in mean maternal cortisol levels and in the distributions of cortisol levels (Levene's test for equality of variances, $F = 1.12$, $p = 0.29$). Further, these cortisol levels were similar to those of women from other cohorts who were assessed at 6−12 weeks postpartum [49,50]. Ratings of infant fear did not differ between the two groups and the means were consistent with ratings of fear in infants during the first year of life from other studies using this scale [2,31,51].

Three of the maternal variables listed in Table 1 reached the criterion ($p<0.1$) for entry as covariates in subsequent hierarchical regression analyses because of their association with infant fear: employment status ($t = 2.5$; $p<0.05$), maternal age ($r = 0.11$; $p = 0.09$) and parity ($t = −1.7$; $p = 0.09$). Maternal education, ethnicity, income and marital status did not reach criteria for inclusion (all $p > 0.22$). In addition, because ratings of infant temperament depend in part on the age of the infant [2] and were modestly associated with temperament ratings in the current sample ($r = −0.13$; $p < 0.05$), in all analyses, infant age was entered as a covariate. Ratings of infant temperament were not related to sex of the infant ($t = 0.56$; $p = 0.57$).

3.2. Maternal cortisol and infant temperament

Among women who were breastfeeding, there was a positive association between maternal cortisol levels and reports of infant fearfulness (partial correlation; $r = 0.20$; $p < 0.01$). Those mothers with higher levels of plasma cortisol and thus, higher levels in their breast milk, had infants who were exhibiting increased fearful behavior (see Fig. 1). In contrast, among those who were feeding formula, the association between maternal cortisol and temperament was not apparent (partial correlation; $r = −0.04$; $p = 0.67$).

Because the sample sizes of the two groups were discrepant and thus might account for the different associations between cortisol and temperament, we used the null hypothesis test for the difference between two correlations

Table 2 Hierarchical regression model examining whether maternal cortisol levels account for unique variance in infant fear beyond postnatal maternal affect among breastfed infants ($n = 181$)

	R^2	ΔR^2	β	Partial r
Model 1	0.09[*]			
Infant age			−0.07	−0.07
Parity (birth order)			0.12	0.13
Maternal age			−0.06	−0.06
Employment status			−0.08	−0.08
Perceived stress			0.04	0.03
State anxiety			0.20	0.14
Depression			0.01	0.01
Model 2	0.13[*]	0.04[*]		
Infant age			−0.11	−0.10
Parity (birth order)			0.15	0.16
Maternal age			−0.08	−0.09
Employment status			−0.06	−0.06
Perceived stress			0.02	0.01
State anxiety			0.20	0.14
Depression			0.03	0.02
Maternal cortisol			0.21[**]	0.21[**]

Note: Parity coded 0 = primiparous and 1 = multiparous. Employment status coded 0 = not employed outside the home or on leave from work and 1 = working outside the home.
[*] $p < 0.05$.
[**] $p < 0.01$.

and confirmed that they were in fact statistically significantly different ($z = 1.74$; $p < 0.5$).

3.3. Potential confounding of negative maternal affect

A statistically reliable relation has been reported between maternal affect and maternal reports of infant temperament [52–54]. It also has been shown that psychological states are related to parenting behaviors [52–58] and cortisol levels [59,60]. Thus, it is conceivable that our findings could be spurious (although the fact that the relation was not found among non-breastfeeding pairs already argues strongly against this possibility). In order to address this, a hierarchical regression analysis was conducted in which the measures perceived stress, state anxiety and depression were entered first and then maternal cortisol. Even when maternal affect and maternal demographic characteristics predictive of infant fear, were taken into account statistically, the relation between cortisol and infant fear remained statistically significant with a similar effect size (See Table 2).

4. Discussion

Based on our data, it seems plausible that GC levels in breast milk influence fearful temperament in infants. Specifically, our data suggest that higher levels of postnatal maternal cortisol are associated with reports of increased fearful behavior among breastfed infants. Of course, this study did not directly assess cortisol levels in breast milk — instead, plasma cortisol levels were used as a marker of breast milk

levels. We believe the findings support our proposal that exposure to cortisol in breast milk influences human infant development for the following reasons: 1) the relation between plasma cortisol levels and breast milk levels is fairly high [1] 2) the relation between fear and cortisol only was found to exist among those infants who were breastfed and not among those who were not and 3) adjusting statistically for maternal demographic characteristics, perceived stress, state anxiety and depression did not alter the relation found between cortisol and temperament among the breastfeeding women. Our study was limited by the fact that we relied on maternal reports of infant temperament which are potentially subject to bias [44,61] and by the fact that we did not have measures of mother−infant interaction and so could not evaluate this as a possible contributor to our effects.

Our findings are consistent with the expanding literature documenting lasting influences of prenatal exposure to GCs on emotion regulation. Animal models demonstrate that prenatal exposure to GCs is associated with increased fear and anxiety behavior in offspring [21,22]. Similarly, human fetuses exposed to higher levels of maternal cortisol late in pregnancy have been shown to exhibit more fussing, crying and negative facial expressions as infants [62] and those exposed to synthetic GCs exhibit increased shyness and emotionality during the first 5 years of life [23] and increased aggressive behavior at 6 years of age [63].

In the rodent models, exposure to heightened levels of GCs ingested in milk is associated with decreased fear behavior, whereas we found the opposite patterns in humans [26–28]. It is impossible to determine from the present study whether these differences are due simply to interspecies differences, to differences in timing of exposure (the early post-partum period in rats is more similar to the late prenatal period in humans than to the postnatal period; [64]), to timing of measurement of outcomes, to the degree of GC exposure (the rodent models employed experimental manipulations of GCs while our study examined naturally occurring levels) or to some other factor.

The importance of very early experience in shaping health and behavior across the lifespan has become increasingly well documented [65,66]. It appears that breast milk may provide one additional avenue through which the mother may influence the development of her offspring. The biochemical messages that characterize maternal−fetal communication during the prenatal period may extend into the postnatal period through messages contained in breast milk.

Acknowledgments

References

[1] Patacchioli FR, Cigliana G, Cilumbriello A, Perrone G, Capri O, Alemà GS, et al. Maternal plasma and milk free cortisol during the first 3 days of breast-feeding following spontaneous delivery or elective cesarean section. Gynecol Obstet Investig 1992;34:159−63.

[2] Garstein MR, Rothbart MK. Studying infant temperament via the revised infant behavior questionnaire. Infant Behav Dev 2003;26:64–86.

[3] Levine S. Infantile experience and resistance to physiological stress. Science 1957;126:405–6.

[4] Liu D, Tannenbaum B, Caldji C, Francis D, Freedman A, Sharma S, et al. Maternal care, hippocampal glucocorticoid receptors, and hypothalamic–pituitary–adrenal responses to stress. Science 1997;277:1659–62.

[5] Suomi SJ. Early determinants of behavior: evidence from primate studies. Br Med Bull 1997;53:170–84.

[6] Liu D, Diorio J, Day JC, Francis DD, Meaney MJ. Maternal care, hippocampal synaptogenesis and cognitive development in rats. Nat Neurosci 2000;3:799–806.

[7] Nachmias M, Gunnar M, Mangelsdorf S, Parritz RH, Buss K. Behavioral inhibition and stress reactivity: the moderating role of attachment security. Child Dev 1996;67:191–204.

[8] Anderson JW, Johnstone BM, Remley DT. Breast-feeding and cognitive development: a meta-analysis. Am J Clin Nut 1999;70:525–35.

[9] NICHD Early Childcare Network. Chronicity of maternal depressive symptoms, maternal sensitivity, and child functioning at 36 months. Dev Psychol 1999;35:1297–310.

[10] Gartner LM, Morton J, Lawrence RA, Naylor AJ, O'Hare D, Schanler RJ, et al. Breastfeeding and the use of human milk. Pediatrics 2005;115:496–506.

[11] Britton JR, Kastin AJ. Biologically active polypeptides in milk. Am J Med Sci 1991;301:124–32.

[12] Peaker M, Neville MC. Hormones in milk: chemical signals to the offspring? J Endocrinol 1991;131:1–3.

[13] Bernt KM, Walker WA. Human milk as a carrier of biochemical messages. Acta Paediatrica Supplement 1999;430:27–41.

[14] Grosvenor CE, Picciano MF, Baumrucker CR. Hormones and growth factors in milk. Endocrine Reviews 1992;14:710–28.

[15] Hamosh M. Bioactive factors in human milk. Pediat Clin North Am 2001;48:69–86.

[16] Seckl JR. Prenatal glucocorticoids and long-term programming. Eur J Endocrinol 2004;151:U49–62.

[17] Meaney MJ, Diorio J, Francis D, Widdowson J, LaPlante P, Caldji C, et al. Early environmental regulation of the forebrain glucocorticoid receptor gene expression: implications for adrenocortical responses to stress. Dev Neurosci 1996;18:49–72.

[18] Zarrow MX, Philpott JE, Denenberg VH. Passage of 14C-4-corticosterone from the rat mother to the foetus and neonate. Nature 1970;13:1058–9.

[19] LeDoux JE. Emotion circuits in the brain. Ann Rev Neurosci 2000;23:155–84.

[20] Owen D, Andrews MH, Matthews SG. Maternal adversity, glucocorticoids and programming of neuroendocrine function and behavior. Neurosci Biobehav Rev 2005;29:209–26.

[21] Welberg LAM, Seckl JR. Prenatal stress, glucocorticoids and the programming of the brain. J Neuroendocrinol 2001;13:113–28.

[22] Welberg LA, Seckl JR, Holmes MC. Prenatal glucocorticoid programming of the brain corticosteroid receptors and corticotrophin-releasing hormone: possible implications for behavior. Neuroscience 2001;104:71–9.

[23] Trautman PD, Meyer-Bahlburg HL, Postelnek J, New MI. Effects of early prenatal dexamethasone on the cognitive and behavioral development of young children: results of a pilot study. Psychoneuroendocrinology 1995;20:439–49.

[24] Weinstock M. The potential influence of maternal stress hormones on development and mental health of the offspring. Brain Behav Immun 2005;19:196–308.

[25] Angelucci L, Patacchioli FR, Scaccianoce S, Di Sciullo A, Cardillo A, Maccari S. A model for later-life effects of perinatal drug exposure: maternal hormone mediation. Neurobehav Toxicol Teratol 1985;7:511–7.

[26] Catalani A, Marinelli M, Scaccianoce S, Nicolai R, Muscolo LA, Porcu A, et al. Progeny of mothers drinking corticosterone during lactation has lower stress-induced corticosterone secretion and better cognitive performance. Brain Res 1993;8:209–15.

[27] Catalani A, Casolini P, Cigliana G, Scaccianoce S, Consoli C, Cinque C, et al. Maternal corticosterone influences behavior, stress response and corticosteroid receptors in the female rat. Pharmacol Biochem Behav 2002;73:105–14.

[28] Catalani A, Casolini P, Scaccianoce S, Patacchioli FR, Spinozzi P, Angelucci L. Maternal corticosterone during lactation permanently affects brain corticosteroid receptors, stress response and behaviour in rat progeny. Neuroscience 2000;100:319–25.

[29] Casolini P, Cigliana G, Alemà GS, Ruggieri V, Angelucci L, Catalani A. Effect of increased maternal corticosterone during lactation on hippocampal corticosteroid receptors, stress response and learning in offspring in the early stages of life. Neuroscience 1997;79:1005–12.

[30] Hart S, Boylan LM, Border B, Carroll SR, McGunegle D, Lampe RM. Breast milk levels of cortisol and Secretory Immunoglobulin A (SIgA) differ with maternal mood and infant neuro-behavioral functioning. Infant Behav Dev 2004;27:101–6.

[31] Worobey J, Blajda VM. Temperament ratings at 2 weeks, 2 months, and 1 year: differential stability of activity and emotionality. Dev Psychol 1989;25:257–63.

[32] Goldsmith HH, Campos JJ. The structure of temperamental fear and pleasure in infants: a psychometric perspective. Child Dev 1990;61:1944–64.

[33] Goldsmith HH, Reisner-Danner LA. Variation among temperament theories and validation studies of temperament assessment. In: Kohnstamm GA, editor. Temperament discussed: temperament and development in infancy and childhood. Lisse: Swets & Zeitlinger Publishers; 1986. p. 1–9.

[34] Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol Bull 2004;130:355–91.

[35] Federenko I, Wüst S, Hellhammer DH, Dechoux R, Kumsta R, Kirschbaum C. Free cortisol awakening responses are influenced by awakening time. Psychoneuroendocrinology 2004;29:174–84.

[36] Kulski JK, Hartmann PE. Changes in the concentration of cortisol in milk during different stages of human lactation. Aust J Exp Biol Med Sci 1981;59:769–78.

[37] Keenan BS, Buzek SW, Garza C. Cortisol and its possible role in regulation of sodium and potassium in human milk. Am J Physiol 1983;244:E253–61.

[38] Gwazdauskas FC, Paape MJ, McGilliard ML. Milk and plasma glucocorticoid alterations after injections of hydrocortisone and adrenocorticotropin. Proc Soc Exp Biol Med 1977;154:543–5.

[39] Yeh K-Y. Corticosterone concentrations in the serum and milk of lactating rats: parallel changes after induced stress. Endocrinology 1984;115:1364–70.

[40] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983;24:385–96.

[41] Spielberger CD. State-Trait Personality Inventory (STPI); 1979.

[42] Spielberger CD. Professional Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1988.

[43] Radloff. The CESD scale: a self-report depression scale for research in the general population. App Psychol Meas 1977;1:385–401.

[44] Youngstrom E, Izard C, Ackerman B. Dysphoria-related bias in maternal ratings of children. J Consult Clin Psychol 1999;67:905–16.

[45] Rodbard D, Hutt D. Radioimmunoassays and related procedures in medicine. Vienna: International Atomic Energy Agency, Publishers; 1974. p. 165–92.

[46] Cohen J, Cohen P, West SG, Aiken LS. Applied multiple regression/correlation analysis for the behavioral sciences.

Mahwah, New Jersey: Lawrence Erlbaum Associates, Publishers; 2003.

[47] Li R, Ogden C, Ballew C, Gillespie C, Grummer-Strawn L. Prevalence of exclusive breastfeeding among US infants: the third health and nutrition examination survey (phase II, 1991–1994). Am J Pub Heath 2002;92:1107–10.

[48] Heck KE, Braveman P, Cubbin C, Chavez GF, Kiely JL. Socioeconomic status and breastfeeding initiation among California mothers. Pub Health Rep 2006;121:51–9.

[49] Fleming AS, Ruble D, Krieger H, Wong PY. Hormonal and experiential correlates of maternal responsiveness during pregnancy and the puerperium in human mothers. Horm Behav 1997;31:145–58.

[50] Magiakou MA, Mastorakos G, Rabin D, Dubbert B, Gold PW, Chrousos GP. Hypothalamic corticotropin-releasing hormone suppression during the post-partum period: implications for the increase in psychiatric manifestations at this time. J Clin Endocrinol Metab 1996;81:1912–7.

[51] Räkkönen K, Pesonen A-K, Järvenpää A-L, Strandberg TE. Sweet babies: chocolate consumption during pregnancy and infant temperament at six months. Early Hum Dev 2004;76:139–45.

[52] Pauli-Pott U, Mertesacker B, Bade U, Haverkock A, Beckman D. Parental perceptions and infant temperament development. Infant Behav Dev 2003;26:27–48.

[53] Hart S, Field T, Roitfarb M. Depressed mother's assessments of their neonates' behaviors. Infant Ment Health J 1999;20:200–10.

[54] Mednick BR, Hocevar D, Baker RL, Schulsinger C. Personality and demographic characteristics of mothers and their ratings of child difficultness. Int J Behav Dev 1996;19:121–40.

[55] Jameson PB, Gelfand DM, Kulcsar E, Teti DM. Mother–toddler interaction patterns associated with maternal depression. Dev Psychopathol 1997;9:537–50.

[56] Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: a meta-analytic review. Clin Psychol Rev 2000;20:561–92.

[57] Repetti RL, Wood J. Effects of daily stress at work on mothers' interactions with preschoolers. J Fam Psychol 1997;11:90-108.

[58] Warren SI, Gunnar MR, Kagan J, Anders TF, Simmens S, Rones M, et al. Maternal panic disorder: infant temperament, neurophysiology, and parenting behaviors. J Am Acad Child Adolesc Psych 2003;42:814–25.

[59] Steptoe A, Cropley M, Griffith J, Kirschbaum C. Job strain and anger expression predict early morning evaluations in salivary cortisol. Psychosom Med 2000;62:286–92.

[60] Droogleever Fortuyn HA, vanBroekhoven F, Span PN, Backstrom T, Zitman FG, Verkes RJ. Effects of PhD examination stress on allopregnanolone and cortisol plasma levels and peripheral benzodiazepene receptor density. Psychoneuroendocrinology 2004;29:1341–4.

[61] Paulhus DL. Measurement and control of response bias. In: Robinson JP, editor. Measures of personality and social psychological attitudes. New York: Academic Press; 1991. p. 17–59.

[62] de Weerth C, van Hees Y, Buitelaar JK. Prenatal maternal cortisol levels and infant behavior during the first 5 months. Early Hum Dev 2003;74:139–51.

[63] French NP, Hagan R, Evans SF, Mullan A, Newnham JP. Repeated antenatal corticosteroids: effects on cerebral palsy and childhood behavior. Am J Obstet Gynecol 2004;190:588–95.

[64] Eliner-Avishai S, Brunson KL, Sandman CA, Baram TZ. Stressed-out, or in (utero)? Trends Neurosci 2002;25:518–24.

[65] Gluckman PD, Hanson MA. Living with the past: evolution, development, and patterns of disease. Science 2004;305:1733–6.

[66] Barker DJP. Mothers, babies and health in later life. Edinburgh: Harcourt Brace & Co. Ltd.; 1998.