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Human milk cortisol is associated with infant temperament

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Summary The implications of the biologically active elements in milk for the mammalian infant are largely unknown. Animal models demonstrate that transmission of glucocorticoids through milk influences behavior and modifies brain development in offspring. The aim of this study was to determine the relation between human milk cortisol levels and temperament of the breastfed infant. Fifty-two mother and infant pairs participated when the infants were three-months old. Milk cortisol levels were assessed and each mother completed the Infant Behavior Questionnaire (IBQ), a widely used parent-report measure of infant temperament. Analyses revealed a positive association between milk cortisol and the negative affectivity dimension of the IBQ (partial $r = .37$, $p < .01$). No correlation was found between elevated cortisol levels and the surgency/extraversion or the orienting/regulation dimensions. Further, the positive association between increased maternal milk cortisol and negative affectivity was present among girls ($\beta = .59$, $p < .01$), but not among boys. (Although, the sex by milk cortisol interaction term was not statistically significant, suggesting that these results require replication.) Environmental factors such as maternal demographics and negative maternal affect (depression and perceived stress) at the time of assessment did not account for the positive association. The findings support the proposal that exposure to elevated levels of cortisol in human milk influences infant temperament. The findings further suggest that mothers have the ability to shape offspring phenotype through the transmission of biologically active components in milk.

It has become increasingly clear that a wide range of early exposures to environmental influences have implications for health and development across the lifespan (Barker, 1998). Prenatal and early postnatal experiences have been linked to alterations in basic metabolic and physiological processes such as glucose metabolism, blood pressure regulation and hypothalamic-pituitary-adrenal (HPA) function (Godfrey and

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Barker, 2000; Phillips and Jones, 2006) and also to the development of a range of disease states including hypertension, coronary heart disease, diabetes, polycystic ovary disease, schizophrenia, depression and anxiety disorders (Van Os and Selten, 1998; Gunnell et al., 2003; Indredavik et al., 2003; Gale and Martyn, 2004; Mittendorfer-Rutz et al., 2004; Seckl and Meaney, 2006).

Despite the well-established and widespread benefits of breastfeeding on health and development (Davis, 2001; Friedman and Zeiger, 2005; Schack-Nielsen and Michaelsen, 2006), little consideration has been given to the possibility that biological components of maternal milk may be an important aspect of the early environment that shapes offspring phenotype (Glynn et al., 2007; Hinde and Capitanio, 2010). Mother's milk contains a wide variety of biologically active hormones — including glucocorticoids (GCs, cortisol in humans; Grosvenor et al., 1992; Hamosh, 2001). GCs are transferred from plasma to milk — there is no evidence for mammary synthesis (Kato et al., 1985; Hamosh, 2001). In human milk, GC levels are lower than in plasma (Pearlman, 1983), but the levels are fairly highly correlated (in the .6—.7 range; Patacchioli et al., 1992). As such, activation of the maternal HPA-axis has implications for milk GC levels. Systemic stimulation with ACTH or exposure to stressors increases GC levels in the milk of cows and rats (Gwazdauskas et al., 1977; Paape et al., 1977; Yeh, 1984). Similarly, maternal milk GC levels have been related to affect and mood in humans (Hart et al., 2004).

GCs are believed to play a critical role in early life programming processes through transmission of signals from mother to fetus (Welberg and Seckl, 2001; Bertram and Hanson, 2002). GCs are stress responsive steroid hormones that are essential for normal development of organ systems, including the central nervous system (Meaney et al., 1996). They easily pass the blood brain barrier (Zarrow et al., 1970) and the limbic regions, such as the amygdala, involved in the regulation of fear, anxiety and behavioral inhibition, are particularly sensitive to their effects (LeDoux, 2000; Owen et al., 2005). Experimental models demonstrate that animals exposed to increased levels of GCs during the prenatal period display increased fear and greater behavioral inhibition in the face of novelty (Welberg et al., 2001; Welberg and Seckl, 2001; Weinstock, 2005). Similar findings during the pre- and early postnatal periods now have been repeatedly documented in human studies (Trautman et al., 1995; de Weerth et al., 2003; Davis et al., 2007; Glynn et al., 2007).

The possibility of lactational programming, the concept that the mother shapes offspring development through signals contained in milk, has been largely ignored. The few studies that have examined this hypothesis are consistent with the premise that milk GCs influence offspring development. Rodent models demonstrate that GCs ingested through milk readily cross the infant's intestinal epithelial barrier and are present in the neonatal plasma and brain (Angelucci et al., 1985). As adults, animals exposed to increased milk GCs during infancy, display altered HPA regulation and

Table 1 Sample characteristics and associations between characteristics and temperament.

	Mother/infant pair (n = 52)	Association with temperament dimensions (p-value)		
		Surgency/extraversion	Negative affectivity	Orienting/regulation
Ethnicity (%)		.37	.33	.61
Latina	21			
Non-Hispanic White	55			
Asian	12			
Other	12			
Maternal age (years; mean)	29.0	.86	.35	.39
Education (%)		.20	.35	.98
High school or less	9			
Associates or technical	33			
College	31			
Graduate	27			
Annual household income (dollars; mean)	68,950	.08	.11	.20
Marital status (% married)	75	.36	.06	.67
Employment (% currently working)	29	.43	.99	.43
Sex of infant (% male)	48	.35	.64	.10
Birth order (% first born)	52	.53	.19	.54
5-minute Apgar score (mean)	9.0	.91	.86	.74
Birth weight (g; mean)	3413	.05	.72	.61
Gestational age at birth (weeks; mean)	39.6	.47	.56	.85
Infant age at assessment (weeks; mean)	13.0	.48	.67	.88
Milk cortisol (μg/dl; mean)	.22			
Temperament (means)				
Surgency/extraversion	3.95			
Negative affectivity	3.07			
Orienting/regulation	5.05			