The Role of Oxytocin in Mother-Infant Relations: A Systematic Review of Human Studies

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Background: **Oxytocin is associated with the establishment and quality of maternal behavior in animal models. Parallel investigations in humans are now under way. This article reviews the current research examining the role of oxytocin in mother-infant relations, attachment, and bonding in humans.** *Methods:* **A systematic search was made of three electronic databases and other bibliographic sources for published research studies that examined oxytocin and mother-infant relations in humans, including attachment, maternal behavior, parenting, and mother-infant relations.** *Results:* **Eight studies were identified, all of which were unique in their methodologies, populations studied, and measures used. Seven studies found significant and strong associations between levels or patterns of oxytocin and aspects of mother-infant relations or attachment.** *Conclusions:* **Oxytocin appears to be of crucial importance for understanding mother-infant relationships. The findings of this review suggest that the pioneering, but preliminary, research undertaken to date is promising and that replication with larger samples is needed. Research that draws on more robust measures of attachment and bonding, as well as improved measures of oxytocin that include both central and peripheral levels, will elucidate the role of oxytocin in human mother-infant relationships. As the production of oxytocin is by no means restricted to mothers, the extension of the oxytocin studies to fathering, as well as to alloparental caregiving, would be an intriguing next step. (Harv Rev Psychiatry 2011;19:1–14.)**

Keywords: **attachment, bonding, mother-infant relations, oxytocin, peptides**

INTRODUCTION

Researchers are becoming increasingly interested in the psychobiology of social affiliation, in general, and in the underlying biology of the mother-infant relationship, in particular. Such research requires an integrative and cross-disciplinary focus, drawing on neuroscience, evolutionary and molecular biology, and social and developmental psychology. The mother-infant relationship in humans consists of a dynamic interaction between maternal caregiving behavior, affective modulation, and cognitive appraisal, and the infant's own pre-programmed signaling and care-eliciting behavior. Whereas the hormonal regulation of the mother-infant relationship has been a focus in animal studies, human studies are still in the initial stages and present a number of methodological challenges.

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Original manuscript received 11 November 2009; revised manuscript received 18 February 2010, accepted for publication 12 April 2010.

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DOI: 10.3109/10673229.2011.549771

Although various related neuropeptides regulate social behavior in vertebrates, oxytocin (OT), along with vasopressin (AVP), evolved with the mammalian linage as a regulator of socio-sexual and reproductive behavior.[1] It has been postulated that OT and AVP have distinct and perhaps even opposing functions, with AVP playing a role in homeostatic regulation of fluid, temperature, and functioning of the cardiovascular and autonomic nervous systems.[2] Through the activation of these systems, AVP may lead to an increase in arousal, attention, and aggression, whereas OT is thought to be more involved in the regulation of prosocial behaviors (with the consequence, for example, that OT may inhibit the actions of AVP during periods such as pregnancy and lactation).[2] Substantial animal research has examined the role of OT in maternal behavior and bonding.[3] Studies in rats, mice, heifers, pigs, and sheep have found an association between OT and maternal behavior.[4–8] Specifically, rat studies using various methodologies have consistently shown an association between OT and maternal behavior. A study of rat pups given either OT or an OT antagonist found that the pups who received OT later (as adults) provided more maternal care to their offspring.[9] In another rat study, maternal care received in infancy was shown to alter central OT receptor expression in the adult rat brain, which, in turn, altered stress activation of the hypothalamic-pituitary-adrenal axis.[9] The most compelling rat studies—which suggest an application to humans—are those showing that rats that have received good maternal care and experienced only brief separations in early infancy have higher OT receptor binding in specific areas of the brain while lactating (the bed nucleus of the stria terminalis, the medial preoptic area, and the lateral septum) than those who received poor maternal care or longer separations as infants.[10–12] Further, in studies of adult female rats that have not had litters, those that received good maternal care in their infancy, when compared to those that did not, had a quicker onset of maternal behavior when exposed to pups and were more responsive to pups.[10] These same rats also had increased estrogen-induced OT receptor levels in the medial preoptic area when they had received higher maternal care in infancy,[10] indicating that a possible model for variations in the quality of maternal care and behavior from one generation to the next is that it is mediated neurobiologically by alterations in the OT system.

Translating observations and findings from animal research into understanding human maternal behaviors is not straightforward. Cross-species comparisons always need to be mindful of differences in the biological function of seemingly analogous behavior. More generally, direct comparison of the reproductive and parenting strategies of humans and other species is often difficult. At the measurement level, for instance, many studies use the licking grooming/arched-back nursing standard to assess maternal behavior in rats,[11] whereas human caregiving is typically investigated through the direct observation of diverse interactive behaviors between infant and mother, as well as by self-report and interview measures seeking to elicit the underlying psychology of caregiving. Psychological measures focus on wide-ranging aspects of mother-infant relations, from maternal behaviors and cognitions, to maternal sensitivity,[13] maternal mind–mindedness (that is, a mother's capacity to treat her infant as an individual with a mind and with a capacity for intentional behavior),[14–16] and attachment behaviors in the infant (or the entire attachment behavioral system).[13] In addition, whereas the patterns of early caregiving behavior in animals who show parental care tend to vary within a narrow range, human maternal behavior varies widely according to culture,[17] age,[18] circumstances around delivery,[19,20] social supports in the postpartum,[20] and even neurobiological factors.

A central factor in shaping early maternal behavior in humans is that, at birth, humans are among the most developmentally immature of all primates and thus require significant parental care after birth.[21] Their vulnerability also makes human neonates highly sensitive to their postnatal caregiving environment. Key aspects of infant brain development are "experience expectant" and "experience dependent," with the consequence that the sensitivity of the caregiving is crucial for healthy development.[22,23] The capacity of women to provide early maternal care, however, varies significantly across the population. Poor or unstable early care results in persisting difficulties in forming and maintaining social relationships and in increased vulnerability to depression, anxiety disorders, substance abuse, personality disorders, and adult physical health disorders.[24–27] The quality of a woman's own early maternal care may influence her capacity to provide maternal care;[28,29] a woman's rejection by her mother in childhood is correlated with her own infant's physical avoidance of his or her mother after a brief separation.[29] Despite such findings, however, the mechanism in humans that ensures responsive and intensive maternal care is as yet unclear, as is the reason why mothers vary so widely in their capacity to provide such care. A biological proposition involving neuroendocrinological processes such as alterations in OT functioning have been extrapolated from findings in animal research and proposed by prominent researchers such as Insel,[30] but human studies remain limited.

In humans, OT has been shown to be associated with delivery,[31] lactation,[31] mood regulation,[32] sexual functioning,[33] and parenting behaviors.[21] Emerging studies are providing ever stronger evidence of a link between OT functioning in humans and mother-infant relations. One idea is that increased OT levels across pregnancy facilitates postnatal maternal behavior and the formation of an emotional bond between mother and infant in humans by acting to reduce anxiety and to ameliorate responses to external stresses. Mothers who have a less anxious state of mind are more able to increase their focus on infant care,[34–36] regulate their mood,[32,37,38] and recognize and respond effectively to nonverbal infant cues in the context of a social learning and reward system.[39] Despite the strong animal models for the role of OT in maternal behavior, one of the key questions in understanding the psychobiology of human caregiving and attachment is the degree to which the considerable variation in maternal caregiving can be accounted for through similar biological mechanisms such as the mediating role of OT. Another key question is the extent to which human pregnancy neurobiologically primes a mother for the demanding role of postnatal maternal caregiving and the degree to which this process is influenced by changes in the production and metabolism of OT during the perinatal period.

This review aims to examine the current literature available on OT and mother-infant relations in humans. Given the difficulty in delineating the different aspects of mother-infant relations and the novelty of this research area, we included OT studies on attachment, bonding, and mother-infant relations.

METHODS

Literature Search

A systematic search was undertaken of the electronic databases PsycInfo, EMBASE, and MEDLINE covering the periods 1967–2009, 1980–2009, and 1950–2009, respectively. Key search terms included: maternal behavior, mother-infant relations, object attachment, oxytocin, parenting, and reactive attachment disorder. The search was limited to English-language and human studies. The reference lists of all identified articles were searched for relevant articles. The search also included all relevant textbooks.

Inclusion/exclusion. All abstracts of articles identified in the electronic data base search were reviewed. Studies included were those of original research that investigated in some way the relationship between OT and mother-infant relations in humans. Studies were excluded if they were theoretical discussions of the role of OT, reviews of the literature on the topic, or articles based exclusively on animal research on OT.

Studies. A total of 69 abstracts was identified, of which 8 studies remained after the inclusion and exclusion criteria were applied. A significant proportion of the abstracts identified were either review articles examining theoretical aspects or discussions of animal research.

RESULTS

All eight studies examined distinctly different aspects of the role of OT in mother-infant relations. The studies are presented in Table 1. The studies were all published in the past five years—which indicates the novelty of this area of research. The methodology of the identified studies varied considerably. The study populations ranged from pregnant women, mothers, children, and young women and men. The studies also varied in the particular aspect of mother-infant relations examined: from maternal sensitivity to maternal-fetal attachment, early separation, and maternal behaviors and cognitions. In addition, the method for collecting and analyzing OT levels varied from plasma to urine and also in the assay technique—which makes comparisons difficult and precludes meta-analytic synthesis of the findings.

Pregnant and Postpartum Women

Two studies examined the same sample of pregnant women across three time points—early pregnancy, third trimester of pregnancy, and one month postpartum—using a longitudinal design. The first study, by Levine and colleagues,[43] examined OT across pregnancy and the early postpartum in relation to postpartum maternal behavior and cognitions. The second study, by Feldman and colleagues,[45] examined OT across pregnancy and the early postpartum in relation to maternal-fetal attachment.

In the first study, Levine and colleagues[43] examined 62 pregnant women across pregnancy and first month of the postpartum. Plasma levels of OT were taken in the first and third trimesters, and in the early postpartum. In the third trimester the Maternal-Fetal Attachment Scale[44] (MFAS) was completed. This study found a wide range of levels of OT across the sample, confirming previous studies that suggest that there is no established range for OT in pregnant and postpartum women.[54] Levine and colleagues did identify, however, five distinct typologies for patterns of change in OT levels across pregnancy and early postpartum: levels that remained stable, that decreased, that increased across pregnancy but dropped in the early postpartum, that dropped across pregnancy but increased in early postpartum, and that steadily increased across the three time points. In comparing those with increasing, decreasing, and flat OT levels, the researchers found that increasing levels across pregnancy rather than the actual level across pregnancy was the best hormonal predictor of higher scores on the MFAS in the third trimester.

The MFAS has six subscales: differentiation of self from fetus, interaction with the fetus, attributing characteristics and intentions to the fetus, giving of self,

Table 1. Studies of Oxytocin and the Mother-Infant Relationship in Humans

Study	Design	Sample	Method of OT measurement	Attachment & other psychological measures	Results	Effect size for OT & an aspect of parent-infant relationship
Fries et al. (2005)[40]	Experimental design with case-control groups measuring hormonal response to social & physical interactions with either their mother or an unfamiliar female stranger	$n = 39$ children 18 children had experienced early neglect & were raised in an orphanage for 7–42 months (mean = 16.6) from birth 21 children who had not experienced early neglect were used as a demographically matched control group	Urinary OT & AVP: baseline via 4 separate 12-hour urine samples; urine samples also taken after set tasks OT & AVP measured with HPLC-UV	Interaction with mothers & strangers was for 30 minutes & included regularly timed affectionate interactions	Those reared by biological parents had higher OT levels following interaction with mother than those who had experienced neglect ($F(1,37) = 3.91$; $p = .056$)	Children raised in an orphanage showed moderately lower OT levels than controls when interacting with their current foster mothers: Cohen's $d = .65$; $r = .31$
Meinlschmidt et al. (2007)[41]	Experimental design with case-control groups Double-blind: intranasal administration of OT or placebo control	$n = 19$ German male university students (age range, 20–28 yrs) 9 with early parental separation 10 matched controls	Intranasal administration of OT (24 IU synthetic oxytocin) at 4:30 pm Salivary cortisol was measured using fluorescence immunoassay 1 minute before, then 5, 15, 25, & 35 minutes after, OT administration	Experience of parental divorce or separation resulting in prolonged separation from one parent measured with items derived from Pennebaker & Susman (1988)[42]	OT application resulted in decline on cortisol in controls but "attenuated decline" in subjects who had experienced EPS	Comparison of EPS group to controls on an index of cortisol change showed significant difference with very large effect size: Cohen's $d = 1.30$; $r = .54$ OT-induced change in cortisol increased in EPS subjects & reduced in controls
Levine et al. (2007)[43]	Longitudinal study over 3 time points (1st & 3rd trimester & up to 1 month postpartum), with determination of different typologies of OT levels over the 3 time points	$n = 62$ pregnant, healthy Israeli females 49% primagravidas Mean age = 28.2 yrs, SEM = .62	Plasma OT measured with OT EIA kit	MFAS (Cranley (1981))[44] (total score from 24 items)	No significant correlations of OT levels with MFAS at either early or late pregnancy Group with increasing OT across pregnancy had higher MFAS scores than those with decreasing or flat profiles ($F(2,42) = 8.67$; $p < .001$)	No significant correlation between maternal-fetal attachment & OT levels across pregnancy

Feldman et al. (2007)[45]	Longitudinal study continuing to follow the same sample & same assessment time points as in Levine et al. (2007)[43] (see above) Additional postnatal measures reported	$n = 62$ pregnant, healthy Israeli females 49% primagravidas Mean age = 28.2 yrs, SEM = .62 (same sample as Levine et al. (2007))[43] (see above)	Plasma OT measured with OT EIA kit (same method as Levine et al. (2007))[43] (see above)	15 minutes of interaction in the first month postpartum coded using the Coding Interactive Behavior–Newborn Version (Feldman et al. (1999))[46] & a structured interview (Yale Inventory of Parent Thought & Action)	OT levels in postpartum related to maternal behavior ($r = .28$; $p < .05$), attachment representations ($r = .35$; $p < .01$), infant monitoring ($r = .42$; $p < .001$) OT levels in 1st trimester of pregnancy related to postnatal maternal behavior ($r = .25$; $p = .04$), attachment representations ($r = .28$; $p < .05$), infant monitoring ($r = .34$; $p < .01$)	Correlation between pregnancy OT levels & postnatal mother-infant interactions: $r = .29$ Correlation between postpartum OT levels & postnatal mother-infant interactions: $r = .35$
Tops et al. (2007)[47]	Experimental, within-subjects, double-blind design Administration of cortisol or placebo (only the placebo condition was reported in the present study, as if the study used a cross-sectional design)	$n = 18$ healthy, premenopausal Dutch females Mean age = 41 yrs, SD = 7 Normal cycling or oral contraceptive pill	Cortisol, ACTH, OT Plasma OT measured using radio immunoassay	5-item attachment subscale of the TCI (Cloninger (1994))[48] Also administered the STAI	Attachment correlated to OT ($r = .59$; $p < .01$) No other subscales of the TCI were correlated with OT level	Partial correlation between attachment & OT level after controlling for state anxiety: $r = .71$
Gordon et al. (2008)[49]	Cross-sectional	$n = 45$ male & female Israeli university students who were romantically unattached Mean age = 24.63 yrs, SD = 3.16	OT ELISA plasma kits for OT, ELISA saliva kit for cortisol Single sample collected in the afternoon	Adult Attachment Styles (Brennan et al. (1998))[50] (18- item self-report, scored using attachment, anxiety, & avoidance dimensions) Also used STAI, BDI, PBI (average of mother & father scores)	OT level was negatively associated with depression on the BDI ($r = -.38$; $p < .01$) but not with anxiety OT positively correlated with PBI (mother care: $r = .42$, $p < .01$; father care: $r = .36$, $p < .05$) No significant associations found on the Adult Attachment Styles	Correlation of OT level & parental bonding: $r = .39$; $p < .01$ (as an average of mother & father scores on the PBI)

(Continued on next page)

Table 1. Studies of Oxytocin and the Mother-Infant Relationship in Humans *(Continued)*

Study	Design	Sample	Method of OT measurement	Attachment & other psychological measures	Results	Effect size for OT & an aspect of parent-infant relationship
Strathearn et al. (2009)[51]	Longitudinal study over 4 time points from 3rd trimester until 14 months postpartum; OT levels taken at the 7-month time point pre- & post-play interactions, & neuroimaging at 11-month time point	$n = 30$ first-time mothers 15 secure on the Adult Attachment Interview 15 classified as insecure-dismissing (selected from 61 who met study criteria)	Serum OT was assessed with a liquid phase radio immunoassay before & after a 5 minute 'free play'	Adult Attachment Interview with dynamic-maturational model coding system (Crittenden (2004))[63]	Secure mothers: compared to insecure-avoidant mothers, higher elevation of OT after interacting with their infants In secure attached mothers OT response to interactions at 7 months correlated with activation of the HPA and ventral striatum in response to crying and smiling faces of own-infant at 11 months	Secure mothers showed higher OT response to interaction task Interaction effect over 4 time points: $F = 2.9$; $p = .04$; Cohen's $d = .63$
Bick et al. (2009)[52]	Experimental design with 2 conditions: mother interacts with her own biological child vs. an unfamiliar child	$n = 26$ mothers with children who were 29–54 months of age (median = 40.7 months)	Urine samples for enzyme-immunoassay of OT levels (EIA)	Maternal Behaviour Q-Sort–Short Version (Pederson & Moran (1990))[53] (25-item assessment of mother-child interaction)	Mothers who interacted with unfamiliar children: higher levels of OT Maternal sensitivity: did not differ between conditions but was not analyzed in terms of OT levels	Differences in OT levels post-interaction between biological & unfamiliar children: Cohen's $d = .69$; $r = .33$

ACTH, adrenocorticotrophic hormone; AVP, vasopressin; BDI, Beck Depression Inventory; EIA, enzyme immunoassay; ELISA, enzyme-linked immunosorbent assay; EPS, early parental separation; HPA, hypothalamic-pituitary-adrenal axis; HPLC-UV, high-pressure liquid chromatography with UV detector; MFAS, Maternal-Fetal Attachment Scale; OT, oxytocin; PBI, Parental Bonding Instrument; SD, standard deviation; SEM, standard error of the mean; STAI, State-Trait Anxiety Inventory; TCI, Temperament and Character Inventory.

role taking, and nesting.[44] Levine and colleagues[43] found that the group who showed an increasing OT pattern over pregnancy also obtained higher scores on two of those subscales—namely, differentiation ($p < .001$) and attributing to the fetus (F (2, 42) = 8.00; $p < 0.001$). The differentiation subscale measures the cognitive capacity to differentiate the fetus from self and includes items such as "I enjoy watching my tummy jiggle as the baby kicks inside." The attributing-to-the-fetus subscale includes items such as "It seems the baby kicks and moves just to keep me from resting."[44] These findings might suggest that the pattern with increasing OT is associated with enhancing the pregnant woman's social cognition and conceptualization of her infant.

These findings need to be considered, however, in the light of psychometric and data-analytic limitations. Some concerns have been expressed in the literature about the reliability and validity of using the MFAS subscales;[55] for instance, reliabilities were originally reported to range from Cronbach's alpha .52 to .73, but a confirmatory factor analysis of the scale items did not support the proposed subscale structure.[56] Levine's study reported an acceptable Cronbach alpha coefficient of .86 for the MFAS as a whole. The five different typologies related to OT were constructed inductively and would require replication in a larger sample.

In the second study, Feldman and colleagues,[45] examined the same cohort and time-point assessments but reported on additional measures in the early postpartum of maternal behavior and maternal representations—that is, the cognitive representations of the attachment relationship—using self-report and observational measures, along with plasma cortisol. Feldman and colleagues found no correlation between OT levels and any demographic factor, including breast feeding. This study was the first to report significant correlations between OT levels in the early postpartum and both maternal behavior and maternal representations. High cortisol levels in the early postpartum were found to be negatively related to high-quality maternal behavior. In a hierarchical multiple regression, high OT and low cortisol predicted the quality of maternal behavior in the first month postpartum. This pioneering study was exemplary in using detailed observational assessment of parenting and in examining the combined effects of two important hormones, OT and cortisol.

Both studies used enzyme immunoassay to measure OT levels. The majority of studies of OT levels in humans have used radioimmunoassay techniques.[57–61] A study comparing enzyme immunoassay with radioimmunoassay for plasma OT levels found these methods to be strongly correlated ($r = .90$).[62]

Mothers After the Postpartum

In a study on 26 mothers from various ethnic backgrounds, and using a counterbalanced design, Bick and Dozier[52] observed interactive behavior of the mothers in a computer game with their four-year-old children or with unfamiliar children of the same age. The children were asked to sit on mothers' laps during the game (for about 25 minutes). Physical contact included whispering to each other, counting while holding each others' hands, sitting together while listening to short stories, and playing tickling games. Maternal sensitivity, positivity and closeness, stress and unease, and the amount of time in close physical contact were rated by coders blind for the specific experimental condition. Ratings did not appear to be significantly different in biological versus unfamiliar dyads. The mothers provided urine samples for enzyme immunoassay of OT levels after the interactive game. All of the laboratory visits took place about the same time in the morning.

Bick and Dozier[52] found that OT levels were higher among mothers after interactions with unfamiliar children than following interactions with their own children. This surprising finding was explained by the potential anxiolytic role of OT in lowering the level of stress when one is confronted with a social stressor. Interacting with an unfamiliar child might constitute a more stressful encounter than interacting with the biologically related child, and to require modulation of stress indexed by higher OT production. OT might have lowered mothers' defensive reactions against the unfamiliar child and stimulated maternal, affective behavior despite the absence of both a biological bond and a history of interactive experiences. The authors did not report associations between OT levels and behavioral ratings across or within conditions. Individual differences in level of sensitivity might be correlated with differences in OT levels, as was found by Feldman and her colleagues[45] in mothers during the postpartum period.

Strathearn, Fonagy, Amico, and Montague[51] conducted a modified version of the Adult Attachment Interview (AAI) with pregnant women. They selected 15 mothers with a secure attachment style and 15 with an insecure-avoidant attachment style, classified using Crittenden's dynamic-maturational approach to coding the AAI.[63] At 7 months after birth, the mothers were observed interacting with their babies during a five-minute free-play session, and serum OT was assessed with a liquid phase radioimmunoassay before and after the interactions. At 11 months after birth, the first-time mothers were asked, while in an fMRI scanner, to look at smiling, neutral, and crying faces of their own 7-month-old infants. The specific procedure was that the mothers were exposed to 60 pictures of smiling, neutral, and crying faces in the scanner, half of which were depicting their own infants, and the other half unfamiliar but matched.

Strathearn and colleagues[51] found that after interacting with their infants, secure mothers' serum OT levels were more elevated than those of insecure-dismissing mothers. OT response to the free-play interactions at 7 months was significantly higher in securely attached mothers as measured by the AAI, a result that was strongly correlated with activation of hypothalamus/pituitary region and the ventral striatum in response to smiling and crying own-infant face cues in the scanner at 11 months. These brain regions are considered to be involved in oxytocinergic and dopamine-associated reward processing. These associations were significantly different for secure versus insecure-dismissing mothers. The authors speculated that OT may be one mechanism by which socially relevant cues activate dopaminergic pathways and thus reinforce behavior. Mothers with secure attachment patterns when interacting with their infants may produce more OT, which increases the experience of reward and which may, in turn, contribute to the mother's ability to provide consistent, nurturant care. This hypothesis needs further research in which OT responses are measured simultaneously with brain activation, and in which the quality of interactions during free play is assessed. Also, adult attachment representations should be established with the widely validated Berkeley approach,[64] although the extent to which such additional studies would alter Strathearn and colleagues' findings is open to debate. Despite the need for further research, this study is unique in addressing the role of OT on various levels of maternal functioning and in trying to relate OT levels directly to brain activation.

Nonpregnant Women

Tops and colleagues[47] examined the relationship between OT, cortisol, attachment, and anxiety in 18 adult women who were normal cycling or taking oral contraceptive pills. The study was experimental and used a within-subjects double-blind design in which the participants were examined under two conditions: after being given either cortisol or placebo. The article discussed here, however, reports only on the placebo data examining the relationship between naturally occurring OT and cortisol levels, on the one hand, and attachment and anxiety measures, on the other. The measures used were the temperament scale of the Temperament and Character Inventory, whose four scales are novelty seeking, harm avoidance, reward dependence, and persistence. The reward dependence scale includes a five-item attachment subscale examining the expression and sharing of emotions with friends.[47] Anxiety was measured using the State-Trait Anxiety Inventory. OT was measured by radioimmunoassay techniques. The study found that OT was correlated with the attachment subscale but not with any other temperament scale or with state anxiety. An association between OT and state anxiety was found to be modulated by attachment; that is, when the associations between OT and attachment and between state anxiety and attachment were controlled, a stronger association between OT and state anxiety emerged.[47]

The Temperament and Character Inventory is not designed as an adult attachment self-report questionnaire but as an assessment of temperament and personality. The advantages and limitations of self-report questionnaires of attachment, as compared to the structured interview such as the Adult Attachment Interview, has recently been subjected to a meta-analytic approach: the association between security measured by the AAI and security in self-report attachment style was found to be very small (mean $r = .09$).[65] The study by Tops and colleagues[47] used a measure of attachment that is another step removed from the self-report methodology and relies on the association found in some studies between personality characteristics and attachment scores on self-report attachment measures. For instance Chotai and colleagues[66] found that the reward dependency scale of the Temperament and Character Inventory correlated positively with secure attachment using the Attachment Style Questionnaire (partial correlation coefficient $r = .22$). The manner in which the study by Tops and colleagues[47] operationalized the construct of attachment consequently limits its conclusions.

Children

A study by Fries and colleagues[40] compared children who had experienced early neglect and institutionalization but subsequent adoption into families ($n = 18$) and children who were reared by their biological parents ($n = 21$). Children had periods of 30-minute interactions with either their mothers or unfamiliar females, with timed physical contact. Urine was collected after the task, and each assessment was separated by at least seven days. In addition, the first urine of the day was collected over four days; the result was averaged to arrive at an estimate of basal OT levels. Compared to those who had experienced early neglect, children reared by their biological parents tended to show higher OT levels after interactions with their mothers, although the association failed to reach conventional alpha level ($p = 0.056$). The groups showed no differences after interacting with the female stranger, and their basal OT levels were also the same.

These children were, on average, around four years of age. The neglected children had spent an average of 16.6 months immediately after birth in orphanages and had spent on average of 34.6 months (range, 10–48 months) with their adoptive parents. Socioeconomic variables in the parents were controlled for, and developmental disability was excluded. The authors included no assessment of parent-child relations in either the neglect or control group and also no information on parental variables such as maternal depression.

The study used radioimmunoassay techniques to assess OT levels in the urine. Early studies (1964, 1973) that compared urinary and plasma measures of OT found significant discrepancies in results,[67,68] but in a more recent study (1987) using OT infusion, radioimmunoassay measurements of OT in plasma and urine were found to be comparable, with urinary and plasma levels related.[69] Although this same study also found that random samples of urine were poorly related to plasma levels (only a small fraction of OT was found to be being cleared in the urine, and the number of subjects was small), the authors concluded that measurement of urinary OT was sensitive to variations in OT levels during infusion.[69] Since this latter finding leaves it uncertain whether urinary basal OT levels are reliable, it raises questions about Fries and colleagues' finding[40] of no difference in basal OT levels. Indeed, Anderson[70] has raised concerns about the urinary measures of OT used in the Fries study, about the sensitivity of the specific techniques used, and about the inconsistencies between the OT levels found in that study and other data on OT levels. He therefore argued that the urinary OT findings of the Fries study should be "disregarded."

Young Adult Men

Meinlschmidt and Heim's study[41] of nine young men with a history of early parental separation (EPS) and ten controls examined the response to double-blind, intranasal OT or placebo. The measures included a self-report questionnaire on five types of early childhood trauma. The authors categorized these traumas as follows: traumatic sexual; divorce or separation of parents; death of family member or close friend; victim of violence; and "other."[42] Those who reported permanent or prolonged separation from a parent before age 13 years were included in the EPS group. Those included in controls reported no category of childhood trauma. Samples of salivary cortisol, measured and analyzed using fluorescence immunoassay, were taken before and at four time points after OT or placebo was administered. Following administration of OT, EPS subjects experienced an increase in salivary cortisol, whereas controls experienced a significant decrease. The pattern of cortisol over time also differed in EPS subjects, compared to controls, following OT administration: the decline was more attenuated in EPS subjects.

It is difficult to draw definite conclusions about OT levels from this study. It was not specifically about mother-infant relations; the separation could be from either parent and at any age under 13 years. It did not directly examine OT levels. It did not provide details of the circumstances surrounding the early parental separation (with the consequence that it is unclear whether the separation was from the primary caretaker for all subjects). And the numbers in each group were small. However, like the study by Fries and colleagues,[40] this study by Meinlschmidt and Heim[41] does suggest a potential link between the quality of early parental care and later OT functioning.

Interestingly, this study used salivary cortisol to examine the effects of centrally administering OT, whereas all other studies identified for this review measured peripheral OT levels. No studies in this review directly measured central OT levels—for instance, through cerebrospinal fluid levels (which is no doubt due to the invasive nature of central measurement for research participants). No existing studies show that centrally administered OT exerts direct effects on OT receptors or even that it acts on other neurotransmitter systems.[41] A review of peptides and their capacity to cross the blood-brain barrier indicated only that it is likely, despite some uncertainty, that peptides, including OT, are capable of crossing.[71] The correlation between central and peripheral levels of OT and the effects of centrally administered OT on receptor regions have yet to be established. Qualifications notwithstanding, Meinlschmidt and Heim's study,[41] which examines the effects of early adversity through central administration of OT rather than by measuring peripheral levels of OT, adds to the overall evidence that OT plays a role in human attachment.

Young Adults

Gordon and colleagues[49] examined 45 young adults (21 men and 24 women) who were not romantically attached. They examined plasma OT and salivary cortisol (both taken in the afternoon) and four self-report measures: State-Trait Anxiety Inventory, Beck Depression Inventory, Adult Attachment Styles, and the Parental Bonding Instrument. OT and cortisol were both analyzed using enzyme immunoassay techniques similar to that used by Levine and colleagues[43] and Feldman and colleagues.[45] Eighteen participants had blood drawn twice to confirm the stability of OT during the experimental period. Psychological distress was found to be negatively associated with OT levels, and bonding was found to be positively associated with OT. Cortisol levels were associated with attachment anxiety but not with attachment avoidance (as measured by the Adult Attachment Styles questionnaire), and there was not a significant association with OT. As previously discussed it remains uncertain whether self-report questionnaires, which predominantly focus on current adult relationships, are comparable to the Adult Attachment Interview, which explores the childhood parental relationship in relation to adult attachment state of mind.[72] This study's finding of no association between attachment and OT may consequently reflect the nature of the attachment assessment. What the study does provide is preliminary data that early parental relationship, vulnerability to depression/anxiety, and OT may be related.

DISCUSSION

Research on early mother-infant relations has predominantly been focused on social and psychological factors that may contribute to the quality of early maternal care. The large literature in animal research suggests, however, that biological factors contribute strongly to both the quality of maternal care of infants and the intergenerational transmission of the motivation and capacity to provide care to infants. Far fewer studies examine directly the biological systems known to be involved in the human attachment and caregiving systems. The planning and design of such studies is difficult and challenging because of the complex interplay of behavioral, psychological, and biological levels of analysis.

Assessment of attachment has evolved over five decades and now includes numerous different measures and methods of assessment such as experimenter-rated observations, laboratory-based experimental procedures, self-report questionnaires, narrative-based play tasks, and structured interview methods. Although the validity and reliability of these various instruments across the human lifespan continue to be matters of investigation and debate, robust findings link the assessment of attachment in mothers (even while still pregnant) using the Adult Attachment Interview with the transmission of these attachment patterns to their infants assessed using the Strange Situation Procedure.[13]

One of the general limitations of current research on OT in humans involving intergenerational transmission of attachment is that no studies have included in their methodology the more established and extensively validated measures of adult and infant attachment in order to examine the role of neuroendocrinological indices such as OT in the development of attachment. Equally, little of the developmental research methodology used in the observation and assessment of mother-infant interaction over the first 12 months has been integrated into neuroendocrinological research. With regard to observed maternal behavior, one study—the pioneering investigation by Feldman and colleagues[45]—did apply, among other micro-analytic measures, the Yale Inventory of Parent Thought and Action, which is a valid observational measure. Bick and Dozier[52] observed interactive maternal behavior during a game and used, among other measures, the maternal behavior Q-sort for sensitivity. In two studies—by Meinlschmidt and Heim[41] and by Strathearn and colleagues[51]—the participants' experience of being parented was assessed. Nevertheless, we still have a long way to go before we understand the role of OT in initiating and maintaining human maternal behavior, in generating affective and motivational states associated with caregiving, in forming social bonds, and in transmitting maternal behavior intergenerationally.

Significant measurement issues also need to be addressed. Within the eight identified studies, seven measured OT peripherally, and one measured cortisol in response to intranasal OT administration. No studies identified directly measured central OT levels—for instance, through cerebrospinal fluid levels. The correlation between central and peripheral OT is uncertain since two studies of pregnant women have found no correlation between CSF and plasma OT levels.[57,73] No differences in CSF OT levels in pregnant versus nonpregnant women have been identified.[57] Given that OT is produced both centrally and peripherally, further investigation of the relation between peripheral and central levels of OT is needed in order to understand the accuracy of the peripheral measures and to resolve uncertainty as to the proper manner of measuring OT. Two findings suggest that peripheral OT levels are valid indicators of the functioning of the brain. First, OT levels appear to be stable over time.[43,45] Second, maternal OT levels have been correlated with activation of hypothalamus/pituitary region and the ventral striatum in response to smiling and crying pictures of their own infants.[51]

An accumulating body of research on diverse aspects of human behavior points toward a potential link between neuroendocinological changes and maternal behavior in humans. While this research is not directly about attachment, it suggests that OT levels and the responsiveness of the oxytocinergic system to emotional stimulation varies considerably from one individual to another.[61] Evidence also suggests that OT in humans alters response to stress[36] and aids in reading nonverbal social cues[39]—both of which are potentially important aspects of early maternal-infant interactions and key components of the attachment system. OT has also been demonstrated to facilitate interaction with an unfamiliar child. This finding suggest that OT has a role in the transition from the first stages of interacting with the newborn baby to establishing a bond during the weeks and months after this initial period.[52] Finally, a recent genetic study found that a gene-by-gene interaction between polymorphisms in OT receptor and serotonin transporter genes was significantly associated with maternal sensitivity.[74]

Although the research in understanding the contribution of neuroendocrinological factors to mother-infant relationship is still in its early stages, some preliminary theoretical models can be proposed for future testing. A distinction needs to be drawn between two different aspects of development: first, the development of infant attachment patterns across the infant's first few years of life, and second, the influence of such patterns on a mother when she is called upon to provide maternal care in adulthood.

In infancy, the evidence from animal studies suggests that central OT receptors are pruned on the basis of the quality of maternal care provided.[10–12] This process has been referred to as a form of early epigenetic programming, which suggests that variation in infants' attachment patterns may be underpinned by neural receptivity to OT release.[75] Since OT release is thought to reduce anxiety by reducing amygdala activation and dampening hypothalamic-pituitary-adrenal activity, it may play an anxiolytic role in the regulation of mood and social stress. Differences in infant attachment patterns may reflect different degrees of central receptivity to OT production or, indeed, different levels of OT production. These comments are speculative since the role of individual differences in OT receptivity or production and the relationship of these differences to infant attachment patterns have not yet been investigated in humans. Further research is needed.

More research has been conducted on the regulation of maternal behavior via the OT system across the perinatal developmental period. Thus, when a woman becomes pregnant, the OT produced by both the mother and her fetus across pregnancy is likely to be a factor influencing the motivational and affective process that is referred to as antenatal bonding. In particular, Feldman and colleagues[45] found strong evidence to support this aspect of the theory. They also found evidence of associations between changes in OT levels across pregnancy and the quality of maternal care such as the maternal bonding behaviors and maternal representations of the relationship. Biologically speaking, priming of maternal brain systems for maternal behavior involves an interaction between the oxytocinergic system and the mesolimbic dopamine reward circuit across pregnancy and the postpartum period.[10,11] Some evidence for this interaction comes from the Strathearn and colleagues' study[51] linking OT response following mother-infant interactions with elevated activity in those areas of the brain. OT produced both centrally and peripherally is released over the course of pregnancy and in substantial amounts during delivery.

OT production in mothers is maintained postnatally by lactation and also in response to innate infant behaviors such as suckling, clinging, facial expressions, and vocal calls.[76,77] The location of OT receptors in the human brain suggests that in the infant, attachment-eliciting signals may act as cues to central OT release that is reinforced, in turn, via an interaction with dopamine-associated brain pathways. OT release in the mother is assumed to have an inverse relationship to stress responses. Since OT release is rapid in response to external stimulation and has effects on the limbic system and orbitofrontal cortex, it acts to potentiate a response to a range of pro-social behaviors, including facial recognition, social memory, and trust—all of which are theoretically associated with maternal caregiving behavior and the dyadic function of the attachment system.

Finally, one of the central hypotheses of attachment theory is that the infant's attachment system serves as a foundation for a future caregiving behavioral system, and high concordance has been found for such intergenerational transmission of attachment patterns. A complete theory of OT's role in human attachment would therefore need to combine these two models of infant attachment and maternal caregiving. Attachment theory suggests that the priming of the maternal caregiving system through infant interaction may itself be building upon a neurobiological basis of OT receptivity that was laid down during mother's own infancy and that, in itself, is a product of her own experience of caregiving. Attachment theory does not suggest that the attachment relationship would be dependent on pregnancy, postnatal lactation, or feeding, as it assumes that infants develop attachment relationships with their mothers, fathers, and other caregivers if they interact on a regular basis. Since the production of OT is by no means restricted to mothers, extending OT studies on mothering and mother-infant attachment to fathering and father-infant attachment, as well as to all parental caregivers, is a fascinating next research step. The first study along these lines has recently been published.[78]

The foundation of attachment reflects the interaction of psychological and biologically co-evolved processes between parent and infant that remain poorly understood. Moreover, in view of the limited amount of research on OT in humans, we can no more than speculate at present about OT's role in human development. The first wave of pathbreaking studies reviewed here, however, strongly suggests that OT has an important role in the development and regulation of parent-infant relationships in humans.

The authors wish to thank Harry Georgiou for his advice and for the information he provided about measurement methods for oxytocin; Michelle Leech for her invaluable advice regarding critical appraisal of research methodology; and the Fellows and Faculty of the 2010 International Psychoanalytic Association Research Training Program held at University College London—and in particular, Peter Fonagy, Robert Emde, and Patrick Luyten.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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