Hormones and Behavior 58 (2010) 669–676

Contents lists available at ScienceDirect

Hormones and Behavior

journal homepage: www.elsevier.com/locate/yhbeh

The cross-generation transmission of oxytocin in humans

Ruth Feldman *, Ilanit Gordon, Orna Zagoory-Sharon

Department of Psychology and the Gonda Brain Sciences Center, Bar-Ilan University, Ramat-Gan, Israel 52900

ARTICLE INFO

Article history:
Received 12 May 2010
Revised 4 June 2010
Accepted 7 June 2010
Available online 15 June 2010

Keywords:
Oxytocin
Parenting
Parent-infant relationship
Synchrony
Social engagement

ABSTRACT

Animal studies demonstrated that the neuropeptide oxytocin (OT), implicated in bond formation across mammalian species, is transmitted from mother to young through mechanisms of early social experiences; however, no research has addressed the cross-generation transmission of OT in humans. Fifty-five parents (36 mothers and 19 fathers) engaged in a 15-min interaction with their infants. Baseline plasma OT was sampled from parents and salivary OT was sampled from parents and infants before and after play and analyzed with ELISA methods. Interactions were micro-coded for parent and child's socio-affective behavior. Parent and infant's salivary OT was individually stable across assessments and showed an increase from pre- to post-interaction. Significant correlations emerged between parental and infant OT at both assessments and higher OT levels in parent and child were related to greater affect synchrony and infant social engagement. Parent–infant affect synchrony moderated the relations between parental and infant OT and the associations between OT in parent and child were stronger under conditions of high affect synchrony. Results demonstrate consistency in the neuroendocrine system supporting bond formation in humans and other mammals and underscore the role of early experience in shaping the cross-generation transmission of social affiliation in humans.

Introduction

Among the central features of the oxytocinergic system, which plays a key role in processes of bond formation across mammalian species, is its sensitivity to early social experience, particularly to variations in parental care (Gimpl and Fahrenholz, 2001; Keverne and Curley, 2004; Lee et al., 2009; Meaney, 2001; Pedersen, 2004; Ross and Young, 2009). Studies in rats, voles, sheep, and non-human primates have shown that maternal Oxytocin (OT) is associated with the provision of maternal behavior and the amount of maternal behavior, in turn, shapes the infant's OT expression and bears long-term consequences for the development of social competence, aggressive behavior, and the infant's ultimate skill as a parent (Carter, 1998; Francis et al., 2000; Keverne and Kendrick, 1992; Maestripieri et al., 2009; Meaney, 2010; Neumann, 2008; Ross and Young, 2009). Rat mothers who provided high levels of licking-and-grooming showed higher OT receptor densities in brain areas central for parenting, including the medial preoptic area, lateral septum, the paraventricular nucleus of the hypothalamus, and the nucleus accumbens. Their female infants similarly engaged in high licking-and-grooming parenting to their own infants and exhibited the brain profile typical of the high licking-and-grooming dams (Champagne, 2008; Francis et al., 2000; Meaney, 2001). Among rhesus monkeys, mothers who provided more grooming and contact had higher levels of plasma OT (Maestripieri et al., 2009), while infant monkeys reared by their mothers showed greater CSF OT concentrations as compared to nursery-reared animals and displayed more social behavior toward conspecifics (Winslow et al., 2003). OT knockout mice expressed less ultrasonic vocalizations in infancy and more aggression and social dysfunction in adulthood (Winslow et al., 2000). Overall, these studies suggest a bio-behavioral feedback loop of OT, parenting, and infant social competence: between maternal OT and the mother's parenting behaviors, between maternal behavior and the infant's OT expression, and between infant OT and the child's life-long capacity for social affiliation, stress management, and adaptation to the social group, a cycle which repeats in the next generation (Ahern and Young, 2009; Champagne et al., 2008; Francis et al., 2000, 2002).

Searching for the mechanisms that underpin the cross-generation transmission of the OT bio-behavioral feedback loop, studies have shown that the transmission of OT and parenting from one generation to the next are based on behavioral and ecological mechanisms to a greater extent than on genetic ones. The seminal work of Meaney and colleagues with cross-fostered animals demonstrated that female infants bred to a high licking-and-grooming brand and reared by low licking-and-grooming dams and vice versa exhibited both the brain profile and ultimate parenting behavior typical of the adopted strain, underscoring the central role of early experience in organizing the structural and functional features of the oxytocinergic system (Champagne and Meaney, 2001; Meaney, 2001). In general, the body

* Corresponding author. Fax: +972 3 535 0267.
E-mail address: feldman@mail.biu.ac.il (R. Feldman).

0018-506X/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.yhbeh.2010.06.005

of research on the cross generation transmission of OT and social affiliation in mammals highlights three main points. First, variations in the early social environment, in maternal behavior, alloparental care, and the nature of the rearing environment (e.g., single mothers versus couple rearing), are related in systematic ways to both the amount of positive parenting behavior the infant receives and the level of parenting the infant will ultimately provide as a parent (Ahern and Young, 2009; Gimpl and Fahrenholz, 2001). Second, parenting behavior shapes the infant's social adaptation through complex gene-by-environment interactions and epigenetic influences that augment the expression of certain genes while downplaying the role of others (Champagne, 2008; Meaney, 2010; Weaver et al., 2004). Finally, the species-specific repertoire of parenting behavior the infant experiences is closely related to the first social behaviors the infant expresses. These early social behaviors are thought to initiate a cascading bio-behavioral process that shapes the infant's lifetime socialization and sets the long-term expression of stress and affiliation neuroendocrine pathways (Feldman, in press; Fleming et al., 1999).

Although less research examined the associations between OT and parenting in humans, recent studies point to consistencies in the neuroendocrine systems that support bond formation in humans and other mammals. For instance, maternal OT levels measured across pregnancy and the postpartum showed high individual stability over time and OT levels at the first trimester predicted the amount of maternal postpartum behavior, including maternal gaze at infant face, "motherese" vocalizations, expression of positive affect, and affectionate touch (Feldman et al., 2007). Similarly, maternal OT was associated with the mother's sensitive behavior toward her infant and with an increased BOLD fMRI response to infant stimuli in brain areas rich in OT receptors (Strathearn et al., 2009). Comparable levels of plasma OT were found in mothers and fathers across the first 6 months of parenting and maternal and paternal OT were related to the parent-specific set of parenting behavior (Gordon et al., 2010). Mothers and fathers who provided high levels of tactile contact to their infants showed an increase in salivary OT following parent–infant interactions but such an increase was not observed among parents who provided low tactile contact (Feldman et al., 2010), echoing the high and low licking-and-grooming patterns of rat mothers and their differential impact on OT expression. OT inhaling increased fathers' response to their toddlers, particularly the father-specific pattern of exploratory play (Naber et al., 2010), and variations in the OXTR gene were related to the degree of maternal sensitivity (Bakermans-Kranenburg and van Ijzendoorn, 2008). Taken together, these studies demonstrate that measures of both central and peripheral OT are reliably linked to meaningful differences in parenting behavior in humans, similar to their role in other mammals.

In addition to its contribution to human parenting behavior, research has demonstrated the relations between lower levels of OT or blunted OT response and conditions associated with disrupted parenting or maladaptive early environments. Lower urinary OT was found in children reared in severely neglectful orphanage conditions as compared to children reared in typical environments (Fries et al., 2005). Women with a history of childhood abuse had lower CSF OT concentrations (Heim et al., 2009), cocaine abusing mothers showed lower plasma OT and more negative affect toward their infants (Light et al., 2004), and maternal postpartum depressive symptoms were related to lower plasma OT and less maternal behavior (Feldman et al., 2007). Studies employing the OT inhaling paradigm showed the effects of OT on social adaptation throughout life, including increased trust (Kosfeld et al., 2005), more responsive couple interaction (Ditzen et al., 2009), decreased social fear (Kirsch et al., 2005), and improved social skills among autistic individuals (Andari et al., 2010). Combined with the well-known links between sensitive parenting in infancy, infant attachment security, and the child's social adaptation up until adulthood (Sroufe, 2005; Bakermans-Kranenburg and van Ijzendoorn, 2007), these studies support each component of the OT bio-behavioral feedback loop: between OT and parenting, between parenting behavior and the infant's social repertoire, and between OT and the individual's social adaptation throughout life. However, the links between all components of the cross-generation transmission cycle in humans have not yet been tested in a single study.

In light of the above, the present study had two goals. First, we examined whether OT levels in human parents and infants are interrelated as they are in other mammals. The second goal was to assess whether OT in parent and child is associated with the parenting behavior the infant receives and the early social repertoire the infant expresses. In addition, we tested whether parenting behavior moderates the relations between the parent's and the infant's OT. Parents (mothers and fathers) and their 4- to 6 month-old infants were observed in a 15-min play session and salivary OT was sampled from parent and child before and after interactions, in addition to baseline plasma OT sampled from the parents. Carter and colleagues (2007a,b) showed that salivary OT is a reliable biomarker of peripheral OT and studies have demonstrated that salivary OT increases after massage in adults (Carter et al., 2007a,b), following affectionate touch between couples (Holt-Lunstad et al., 2008), and after a session of parent–infant contact (Feldman et al., 2010), pointing to the links between salivary OT and processes of social affiliation.

Several hypotheses were proposed. Consistent with research in animal models (Champagne and Meaney, 2001), we hypothesized that parental and infant's OT, at both the baseline and post-interaction assessments, would be significantly correlated and higher parental OT would be related to higher infant OT. It was further expected that more sensitive parenting behavior would be associated with higher parental and infant OT. Specifically, we expected correlations between parent–infant synchrony and higher levels of parental and infant OT. Parent–infant synchrony indexes the parent's capacity to carefully monitor and adapt to micro-level shifts in the infant's socio-affective signals and to enter into a matched social dialogue with the child (Feldman, 2007a,b). In addition, the infant's social engagement, addressing the infant's early non-verbal social repertoire, is an important marker of social development and has shown to predict greater social competence with peers (Feldman and Masalha, 2010; Marshal and Fox, 2006). We thus expected that higher parental and infant OT would be related to more infant social engagement. Finally, studies in animals indicate that infants reared in positive environments benefit more from environmental enrichment (Curly et al., 2009; Ross and Young, 2009), suggesting that positive early experience may enhance the cross-generation transmission of OT. We thus examined whether parent–infant synchrony would moderate the relations between the parent and infant's OT so that among infants reared under conditions of high affect synchrony a closer relationship would be observed between the parent's and the infant's OT as compared to infants reared under conditions of low affect synchrony.

Method

Participants

Participants were 55 parents, including 36 mothers and 19 fathers (not couples) and their 4- to 6-month-old infants (M = 157.1 days, SD = 11.9). All parents were healthy with at least 12 years of education and were of middle-class SES. Mothers were on average 28.3 years (SD = 5.11), completed on average 15.45 (SD = 2.83) years of education, and 82.5% of the mothers were breastfeeding. Fathers' age averaged 29.6 years (SD = 4.78) with an average education of 15.58 (SD = 2.82) years. Infants were born at term, mainly (92%) by vaginal delivery, and received an Apgar score of 9.12 (SD = 1.43). Sixty-one percent of the infants were firstborn. Fathers reported at least medium-level participation in childcare. To screen for parental mood disorders, parents completed the Beck Depression Inventory (Beck,

1978) and the State-Trait Anxiety Inventory (Spielberger, 1984). Parents with a score of 11 and above on the BDI or 44 and above on the STAI, indicating risk for anxiety or depression disorders, were not included in the study.

Procedure

Parents and infants arrived at the lab between 1 and 4 PM and visits were coordinated to the period between 1 h following the last breastfeeding and 1 h prior to the next breastfeeding. The timing of the visit was set in accordance with research by White-Traut et al. (2009), who showed that salivary OT was highest within 30 min before breastfeeding, decreased at the initiation of feeding, and increased 30 min after breastfeeding. Similarly, previous research indicated that OT peaks in the early morning and declines until noon (Amico et al., 1989) and thus, we chose to sample OT in the early afternoon to minimize the effects of diurnal changes on OT reactivity. Following a 10-min familiarization period when no touch between parent and child occurred, parents provided baseline saliva and plasma samples and salivary samples were collected from the infants. Following this period, parent and child entered a carpeted observation room with an infant-seat mounted on a table and two cameras placed on adjacent walls that were controlled from an adjoined observation room, one focused on the parent, the other on the infant. The two pictures were combined into a single image through a split-screen generator. Parents were asked to engage in a 15-min "play-and-touch" interaction that would include any type of touch they typically use. Fifteen minutes after the end of the session post-interaction saliva samples were collected from parent and child. The study was approved by the Institutional Review Board, all procedures were explained to the parents before the beginning of the study, and all participants signed an informed consent.

Hormone collection and analysis

Plasma oxytocin

Blood was drawn from antecubital veins into a 9-mL chilled vacutainer tubes containing lithium heparin that was supplemented with 400 KIU of Trasylol (Trasylol, Bayer, Germany) per 1 mL blood. Blood samples were kept ice-chilled for up to 2 h before being centrifuged at 4 °C at 1000*g* for 15 min. Supernatants were collected and stored at −80 °C until assayed.

Salivary oxytocin

OT from saliva was collected by Salivattes (Sarstedt, Rommelsdorft, Germany). Parents were asked to chew a roll of cotton for about 40 s. Similarly, a salivette was placed in the infant's mouth to chew for a minute. Salivettes were kept ice-chilled for up to 1 h before being centrifuged at 4 °C at 1500*g* for 15 min. The liquid samples were stored at −80 °C. To concentrate the samples by 3 or 4 times, the liquid samples were lyophilized over night and kept in −20 °C until assayed. The dry samples were reconstructed in the assay buffer immediately before analysis by Oxytocin EIA commercial Kit, consistent with previous research (Carter et al., 2007a,b).

Determination of oxytocin

Determination of OT was performed using a commercial OT ELISA kit (Assay Design, MI, USA) consistent with previous research (Carter, 2007; Feldman et al., 2007; Gordon et al., 2008; Levine et al., 2007). Measurements were performed in duplicate and the concentrations of samples were calculated by using MatLab-7 according to relevant standard curves. The intra-assay and inter-assay coefficient are <12.4% and 14.5% respectively.

In order to provide a reliable comparison between OT concentrations in adults and infants, OT concentrations of parent and infant were normalized to protein. Salivary secretion are important for oral health, accomplishing mechanical cleansing and protective functions through a number of physiological and biochemical mechanisms. During infancy, salivary composition undergoes changes that reflect the maturation of the salivary glands and teeth grow, leading to variability in protein concentration in infants' saliva (Denzan et al, 2002; Sivakumar et al., 2009). The concentration of OT in saliva may depend on the concentration of protein in saliva and since the protein concentration in infant saliva is lower than the protein concentration in adult saliva, salivary OT concentrations of parents and infants were normalized to their protein concentrations. Protein concentration was determined by Bradford assay, using Bio-Rad solution. Parent protein concentration was, M = 0.81 mg/ml (SD = 0.44), at the pre-interaction assessment and, M = 0.76 mg/ml (SD = 0.46), at the post-interaction assessment. Infant protein concentration was, M = 0.37 mg/ml (SD = 0.21) at the pre-interaction assessment and, M = 0.39 mg/ml (SD = 0.22) at the post-interaction assessment.

Coding of parent–infant interactions

Interactions were micro-coded on a computerized system (Noldus, The Vaggenigen, Netherlands), consistent with previous research on parent–infant synchrony (Feldman and Eidelman, 2004, 2007). Four non-verbal categories of parenting behavior and four non-verbal categories of infant behavior were coded and each category included a set of mutually exclusive codes (an "uncodable" code was added to each category in instances during which codes could not be determined). Categories and codes were as follows:

Parent: parent gaze—this category assessed the direction of parent gaze and included the following codes: gaze to infant's face, gaze to infant's body; gaze to object or environment; and gaze aversion, indicating that parent gazes away from the infant but gaze is not focused on other objects or the environment. *Parent affect*—parent's expressed affect was coded on the basis of facial expressions, body tone, movements, and other non-verbal signals and included positive, neutral, and negative affective expression. *Parent vocalizations*—the parent's vocal output was coded along four codes: "motherese" vocalization—infant directed speech that is high-pitched and typically includes sing-song vocalizations; "typical" adult speech to the infant in a normal range and regular rhythm; adult speech to other adult; and no speech. *Parent touch*—included six codes: affectionate touch—loving touch such as hugging, kissing, stroking, or light pokes; touch of infant extremities—touch of infant's hands or feet often with another object; functional touch—touch that has a functional goal such as wiping the infant's mouth; proprioceptive touch includes touch that changes the infant's position in space, for instance, pulling the infant to a sitting position; stimulatory touch, indicates touch that intends to stimulate and increase arousal, and no touch.

Infant: infant gaze–was coded similar to parent's gaze along the following codes: gaze to parent, gaze to object or environment, and gaze aversion. *Infant affect*: was similarly coded as positive, neutral, or negative. *Infant vocalizations*: included positive vocalizations, such as positive babbling, cooing, or giggles, negative vocalizations, including fussing and crying. *Infant touch*—included intentional, accidental, and no touch. Inter-rater reliability was computed for 15 interactions and reliability *kappas* averaged 0.86 (range = 0.77–0.93)

Two composites were computed from the aforementioned codes on the basis of our a-priori hypotheses. *Infant social engagement* was the sum proportions of time the infant was in a social gaze (look at parent) while expressing positive affect and/or positive vocalizations. *Affect synchrony*—was computed as the proportion of time parent and child coordinated their positive engagement and was measured by a conditional probability that indexed the proportion time parent was

Table 1
Descriptive statistics for study variables.

	M	SD	Minimum	Maximum
Parent plasma OT	356.13	135.99	192.61	821.79
Parent salivary OT—pre-interaction	10.46	5.93	2.59	32.65
Parent salivary OT—post-interaction	12.86	8.68	2.06	40.42
Infant salivary OT—pre-interaction	16.37	10.74	1.30	44.36
Infant salivary OT—post-interaction	21.82	16.92	2.37	76.36
Infant social engagement	0.45	0.20	0.08	0.88
Parent–infant affect synchrony	0.27	0.16	0.03	0.76

Note: plasma OT values are in pg/ml, saliva OT values are (pg OT)/(mg protein). Interaction variables represent proportion of time this behavior was observed out of the entire interaction.

in positive affect and "motherese" vocalizations given the infant was in positive engagement.

Results

Results are reported in three parts. In the first, we examined parameters related to OT: individual stability in OT, reactivity of OT to the parent–infant interaction, and correlations between OT levels in parent and child at the pre- and post-interaction assessments. The second part examined correlations between parent and infant's OT and the behavioral measures—Affect Synchrony and Social Engagement. The third part presents a regression equation assessing the moderating role of Affect Synchrony on the relations between parental and infant OT.

OT in parent and infant: stability, reactivity, and parent–child correlations

Prior to data analysis, Pearson's correlations were computed to test potential relationships between the parent and infant's plasma and salivary OT and background variables. No correlations were found between OT measures and demographic variables, including parent age, height, weight, body mass index, smoking, use of medications, and time since last meal. Maternal OT was unrelated to menstrual cycle phase, contraceptive intake, mode of delivery (vaginal vs. c-section), feeding style (breastfeeding vs. bottle-feeding), postpartum interval (weeks from birth to date of assessment), or the interval from prior breastfeeding.

Table 1 presents descriptive statistics for all study variables, including OT levels in parental plasma and saliva at the pre- and post-contact assessments, infant salivary OT at the pre- and post-contact assessments, and the behavioral measures—social engagement and affect synchrony.

No differences in plasma or salivary OT were found between mothers and fathers in the two assessments. Similarly, no differences were found between the OT levels of male and female infants or between infants interacting with mother or father at the two assessments. The distributions of parent and infant OT in the pre- and post-interaction assessment are presented in Fig. 1A and B.

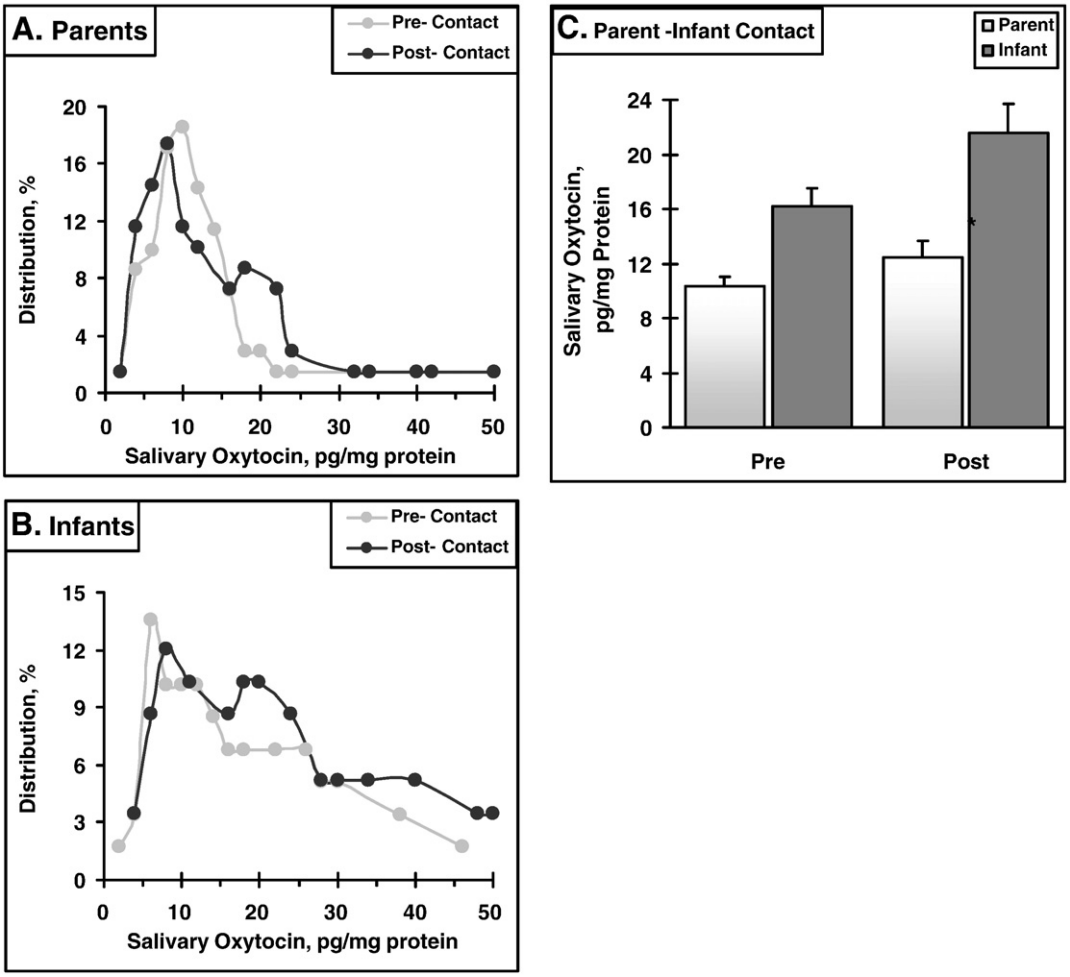

Fig. 1. Salivary OT in parents and infants before and after parent–infant contact. The *x* axis for the pre- and post-contact assessments for parents (A) and infants (B) shows groups for every 5 pg/ml range, presented as the highest value of each range. The *y* axis for A and B shows the number of participants in each range group represented as the percentage of total participants. Means and SE of salivary OT for parents and infants are presented for the pre- and post-parent–infant contact assessments (C).

Baseline OT levels in the parents' plasma and saliva were significantly correlated, $r = 0.46$, $p < 0.001$. These findings indicate that higher plasma OT was associated with higher salivary OT and points to significant co-variance between levels of OT measured in these two systems.

Pearson's correlations were used to examine individual stability in parent and infant's OT across assessments. OT was individually stable from pre- to post-interactions in both parents, $r = 0.55$, $p < 0.001$, and infants, $r = 0.50$, $p < 0.001$. These findings are consistent with previous research demonstrating high individual stability in multiple assessments of OT (Feldman et al., 2007; Gordon et al., 2010; Zak et al., 2004, 2005). In addition, the findings demonstrate that already at the first months of life OT expression is individually stable across assessments.

To examine OT reactivity we assessed changes in OT levels from the pre- to the post-interaction assessments using paired comparison t tests for parent and child. OT in both parent and child increased following the contact interaction: Parent, t $(df = 1, 54) = -2.17$, $p = 0.03$, and infant, t $(df = 1, 54) = -2.65$, $p = 0.01$. These findings are presented in Fig. 1C.

Pearson's correlations were used to examine the associations between the parent's and the infant's OT at the two assessments. Parent and child's OT levels were significantly correlated at both the pre-interaction assessment, $r = 0.45$, $p < .001$, and the post-interaction assessment, $r = 0.48$, $p < 0.001$, and higher parental OT was associated with higher infant OT. These findings suggest that mechanisms of cross-generation transmission in the OT system are observed in human parents and infants in the first months of the infant's life.

Finally, to address OT reactivity, we computed the change in OT for each parent and child by subtracting the pre-interaction levels from the post-interaction levels. OT change in parent and child were significantly correlated, $r = 0.37$, $p = 0.008$, suggesting that the degree of reactivity of the OT system in parent and child is inter-related. OT change in the parent was unrelated to the behavioral measures; however OT change in the infant was marginally correlated with affect synchrony, $r = 0.25$, $p = 0.07$.

Relationship between parent and infant's OT and parent–infant interaction

Pearson's correlations were computed between the parent and infant's OT at the two assessments with Social Engagement and Affect Synchrony. Parent OT following interactions showed significant associations with both Social Engagement, $r = 0.30$, $p = 0.02$, and Affect Synchrony, $r = 0.33$, $p = 0.013$, indicating that higher parental OT is associated with more infant social engagement and greater affect synchrony. Infant OT following interactions similarly correlated with both Social Engagement, $r = 0.41$, $p < 0.001$, and Affect Synchrony, $r = 0.32$, $p = 0.014$, showing links between higher infant OT with more social engagement and synchrony. The parent's pre-interaction OT was marginally associated with more Social Engagement, $r = 0.23$, $p = 0.08$, and was significantly correlated with greater Affect Synchrony, $r = 0.27$, $p = 0.047$. Infant pre-interaction OT was similarly related to more Social Engagement, $r = 0.29$, $p = 0.043$ and Affect Synchrony, $r = 0.27$, $p = 0.048$. Overall, these findings demonstrate significant associations between OT levels in both parent and child with indices of parenting and more infant positive engagement in the interaction and support the hypothesis that early social experiences are related to OT in human parents and infants.

The moderating role of affect synchrony on the relations between parental and infant OT

The final section presents a hierarchical multiple regression equation assessing the moderating role of Affect Synchrony on the relations between the parent's and the infant's OT. The criterion variable was the infant's post-interaction OT. Predictors were entered in four blocks. In the first, parent gender was entered to partial out variance related to parent gender. In the next block, the parent's post-interaction OT was entered, in the third block, Affect Synchrony was entered, and in the final block, the product of parent post-interaction OT and Affect Synchrony. Results are presented in Table 2.

Table 2
Predicting infant salivary OT: the moderating role of affect synchrony.

Predictors	Beta	R	R^2 change	F change	DF
Parent gender	−0.16	0.14	0.02	1.00	1, 53
Parent OT: post-interaction	0.39*	0.46	0.18	11.54**	2, 52
Affect synchrony	0.33+	0.51	0.03	3.67+	3, 51
Affect synchrony × parent OT	0.83*	0.59	0.10	6.56*	4, 50

R^2 Total = 0.34: F $(df = 4, 50) = 5.80$, $p < 0.000$.
*+$p = 0.06$, $p < 0.05$, ** $p < 0.01$.

As seen in Table 2, infant OT was independently predicted by the parent's OT, marginally predicted by Affect Synchrony, and the interaction of parent OT and affect synchrony explained unique variance in the infant's OT, pointing to a moderating effect. Examination of the interaction showed that under condition of low Affect Synchrony (above and below the median split, Median = 0.26) no differences were found in infant OT among infants whose parents had high or low parental OT, F $(df = 1, 22) = 0.86$, p = 0.36. However, under condition of high Affect Synchrony, infants whose parents showed high OT had significantly higher OT than infants whose parents showed low OT, F $(df = 1, 25) = 3.98$, $p = 0.04$. These findings, presented in Fig. 2, point to the moderating role of Affect Synchrony on the relations between parental and infant OT and demonstrate that positive early parenting experience enhances the cross generation transmission of OT in humans, similar to its role in other mammals.

Discussion

This study is the first to assess OT in human infants in relation to the OT response of their parents, the parenting behavior they experience, and the social repertoire they express. Results demonstrate that OT levels in parents and infants are individually stable and both parent and child display the OT response and increase their OT levels after an episode of joint play. Most importantly, parent and infant's OT concentrations showed significant correlations at both the pre- and post-interaction assessments, suggesting a cross-generation transmission of OT in humans similar to that observed in other mammals (Champagne, 2008; Meaney, 2001). Consistent with research in animals, parental and infant's OT levels were related to the degree of contingent parenting and to the infant's social engagement with the parent. These results lend support to perspectives that underscore the centrality of early experience in shaping the

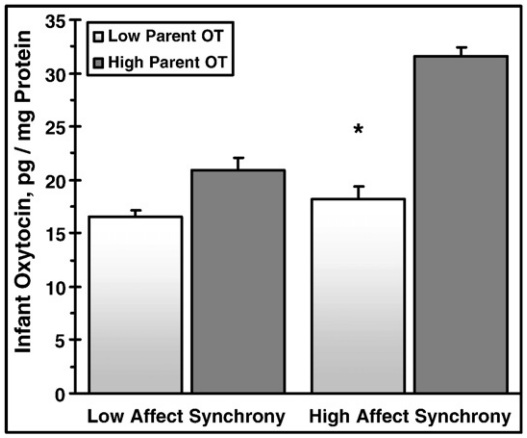

Fig. 2. Salivary OT among infants experiencing high and low affect synchrony in relation to parental OT. $p < 0.05$.

neuroendocrine systems that support bond formation in humans and its important role in the transmission of social affiliation mechanisms from one generation to the next (Meaney, 2010; Ross and Young, 2009). It is important to note, however, that similar to research on the cross-generation transmission of attachment in humans (e.g., Bakermans-Kranenburg and van Ijzendoorn, 2007) our results demonstrate associations between parental and infant OT and the brain mechanisms underlying these transmissions can only be inferred from animal studies. It is possible that adoption research may shed further light on the specific mechanisms of transmission in humans, although such studies often cannot assess OT in the biological parents. In addition, because this study is the first to assess OT in parents and their infants, replications of the findings are required before the results can be generalized.

The findings demonstrate that already in the first months of life, the oxytocinergic system is active in human infants, is measurable, and reacts to social contact in a predictable way. The fact that infant OT showed a high level of individual stability suggests that already in the first half-year of life there may be a consolidation of the OT response that is likely shaped by the infant's earliest social experiences with the parent. Previous studies showed high levels of individual stability in OT concentrations in adults across several months (Feldman et al., 2007; Gordon et al., 2010) and suggested that when not measured during peak experiences, such as nursing or sexual intercourse, OT may represent a relatively stable trait of the individual. The present findings suggest that the formation of this trait-like orientation may begin early in life in relation to the infant's early social provisions.

The correlations between parent and infant's OT at the two assessments suggest that the OT systems of parent and child is interdependent at both baseline functioning and reactivity to a mutual social exchange. Attachment theory postulates that sensitive parenting shapes the infant's lifetime social adaptation through its effects on the infant's environment-dependent brain systems (Bowlby, 1969; Carter et al., 2005). Similarly, research has demonstrated the cross-generation transmission of attachment patterns and showed that individuals who were securely attached to their own parents provided more sensitive parenting to their infants, who, in turn, showed higher attachment security to the parent (Bakermans-Kranenburg and van Ijzendoorn, 2007). The present findings may chart one pathway for the cross-generation transmission of attachment in humans and suggest that a synchronous parent–infant exchange may provide one avenue for the transfer of social affiliation and its biological underpinnings from one generation to the next.

Not only was parent–infant synchrony associated with OT in parent and child, it moderated the relations between parental OT and infant OT. Similar to the effects of social enrichment on the development of the OT system in young mammals (Ross et al., 2009), the data indicate that among infants growing under conditions of high affect synchrony the cross-generation transmission was stronger and closer links were found between the OT levels of parent and child. Because parent–infant synchrony is individually stable across the first year (Feldman, 2007a,b), it is likely that such infants were growing up in environments characterized by high affect synchrony throughout infancy. We suggest that parent–infant synchrony may provide one mechanism by which the neuroendocrine foundation of social affiliation exerts its cross-generation transmission. Synchrony is a concept coined by the first researchers on parenting in social animals. Synchrony describes the coordination of hormonal, behavioral, and physiological stimuli between parent and infant during social contact that provides critical inputs for growth and development of the young (Schneirla, 1946; Rosenblatt, 1965; Wheeler, 1928). Through such bio-behavioral synchrony mammalian mothers adapt their physiological systems to those of the infant's and this process facilitates physiological maturation and social adaptation (Fleming et al., 1999). In humans, parent–infant synchrony appears in a species-typical form that involves the coordination of visual, vocal, and affective signals during social contact and this experience organizes the infant's physiology and prepares for optimal socialization. Moreover, synchrony describes the multi-level mutual influences that occur between the biological processes and social behavior of parent and child: between the biological process of one and those of the other; between the behavioral signals of the two partners that are integrated into the synchronous exchange; and between the biology of one partner and the behavior of the other (Feldman, 2010). As such, synchrony may provide an essential experience for the cross-generation transmission of physiological processes by means of social contact within an attachment relationship.

Infant social engagement was related to OT levels in both parent and child. The infant social engagement construct includes the earliest set of signals that mark the human infant's involvement in a social exchange, such as gaze to partner's face, the expression of positive affect within a social context, and the production of positive communicative vocalizations. Infant social engagement is underlay by specific physiological support systems (Porges, 2003) and a distinct brain circuitry (Johnson et al., 2005) and has shown to predict children's cognitive, social, and emotional growth (Marshal and Fox, 2006). The present findings suggest that social engagement during the period when infants first enter the social world is supported by the oxytocinergic system. Because maternal OT was found to be individually stable from early pregnancy to the first postpartum months (Feldman et al., 2007), it is possible that the parent's OT impacted the infant's OT by means of affect synchrony and that the infant's OT then supported a more engaged and socially competent behavior. These findings point to the importance of detecting conditions associated with reduced parental OT, such as maternal postpartum depression, cocaine use, or early trauma, and providing early intervention before the parent's disrupted OT affects the consolidation of the infant's OT response.

Limitations of the study relate to the fact that no longitudinal data were available to assess predictors and outcomes of the parent and infant's OT. Still, previous longitudinal studies of parental OT, parent–infant synchrony, and infant social engagement may inform the present results. Similarly, data from mother and father of the same infant could have added additional information on the separate and combined contribution of maternal and paternal OT to the infant's OT. Another limitation of the study is the peripheral assessment of OT, which is unavoidable in humans. Although the relations between central and peripheral OT are not fully understood, studies in animals (Wotjak et al., 1998; Carter et al., 2007c; Ross and Young, 2009) and humans (Burri et al., 2008) suggest that central and peripheral activity of the OT system are likely to be coordinated. Research has similarly shown parallel increases in maternal plasma OT and in the mother's fMRI BOLD response to own infant stimuli in brain areas rich in OT receptors (Strathearn et al., 2009) suggesting a parallel in the response of central and peripheral levels. The correlations found here between baseline plasma and salivary OT and between salivary OT in parent and child provide further support for the validity of salivary OT, but further research comparing salivary and plasma OT measured simultaneously is needed to determine the conditions under which OT in these two peripheral systems converge or diverge. Much further research is required to assess OT in infants in relation to other physiological systems, genetic markers, social abilities, developmental outcomes, and high risk parenting in order to describe how the early social environment shapes the infant's life-long capacity to engage in the social world.

Acknowledgments

Research at Dr. Feldman's lab during the study period was supported by the Israel Science Foundation (#1318/08), the US-Israel Bi-National Science Foundation (2005-273), the NARSAD Foundation (Independent Investigator Award, 2008), and the Harris Foundation.

References

Ahern, T.H., Young, L.J., 2009. The impact of early life family structure on adult social attachment, alloparental behavior, and the neuropeptide systems regulating affiliative behaviors in the monogamous prairie vole (microtus ochrogaster). Front. Behav. Neurosci. 3, 17.

Amico, J.A., Levin, S.C., Cameron, J.L., 1989. Circadian rhythm of oxytocin in the cerebrospinal fluid of rhesus and cynomolgus monkeys: effects of castration and adrenalectomy and presence of a caudal-rostral gradient. Neuroendocrinology 50, 624–632.

Andari, E., Duhamel, J.R., Zalla, T., Herbrecht, E., Leboyer, M., Sirigu, A., 2010. Promoting social behavior with oxytocin in high-functioning autism spectrum disorders. Proc. Natl. Acad. Sci. U. S. A. 107, 4389–4394.

Bakermans-Kranenburg, M.J., van Ijzendoorn, M.H., 2007. Research Review: genetic vulnerability or differential susceptibility in child development: the case of attachment. J. Child Psychol. Psychiatry 48, 1160–1173.

Bakermans-Kranenburg, M.J., van Ijzendoorn, M.H., 2008. Oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes associated with observed parenting. Soc. Cogn. Affect. Neurosci. 3, 128–134.

Beck, A.T., 1978. Beck Depression Inventory. The Psychological Corporation, Brace Jovanovich, San Antonio.

Bowlby, J., 1969. *Attachment, vol. 1 of Attachment and loss (2nd edition, 1982)* London: Hogarth Pree; New York: Basic Books.

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

Carter, S.C., Ahnert, L., Grossmann, K.E., Hrdy, S., Lamb, M.E., Porges, S.W., Sachser, N. (Eds.), 2005. Attachment and Bonding: A New Synthesis (Dahlem Workshop Report 92). Boston, MA: MIT Press.

Carter, S.C., Ahnert, L., Grossmann, K.E., Hrdy, S.B., Lamb, M.E., Porges, S.W., Sachser, N. (Eds.), 2007a. *Attachment and Bonding: A New Synthesis* (Dahlem Workshop Report 92). MIT Press, Boston, MA.

Carter, C.S., 2007. Sex differences in oxytocin and vasopressin: implications for autism spectrum disorders? Behav. Brain Res. 176, 170–186.

Carter, C.S., Pournajafi-Nazarloo, H., Kramer, K.M., Ziegler, T.E., White-Traut, R., Bello, D., Schwertz, D., 2007b. Oxytocin: behavioral associations and potential as a salivary biomarker. Ann. NY Acad. Sci. 1098, 312–322.

Carter, C.S., Pournajafi-Nazarloo, H., Kramer, K.M., Ziegler, T.E., White-Traut, R., Bello, D., Schwertz, D., 2007c. Ann N Y Acad Sci. 1098, 312–322.

Champagne, F.A., 2008. Epigenetic mechanisms and the transgenerational effects of maternal care. Front. Neuroendocrinol. 29, 386–397.

Champagne, D.L., Bagot, R.C., van Hasselt, F., Ramakers, G., Meaney, M.J., de Kloet, E.R., Joels, M., Krugers, H., 2008. Maternal care and hippocampal plasticity: evidence for experience-dependent structural plasticity, altered synaptic functioning, and differential responsiveness to glucocorticoids and stress. J. Neurosci. 28, 6037–6045.

Champagne, F., Meaney, M.J., 2001. Like mother, like daughter: evidence for non-genomic transmission of parental behavior and stress responsivity. Prog. Brain Res. 133, 287–302.

Curly, et al., 2009. Social enrichment during postnatal development induces transgenerational effects on emotional and reproductive behavior in mice. Front. Behav. Neurosci. 3, 25.

Denzan, C.C., Nicolaus, J., Souza, D.N., Walter, L.R.F., 2002. Flow rate, amylase activity, and protein and sialic acid concentrations of saliva from children aged 18, 30 and 42 months attending a baby clinic. Arch. Oral Biol. 47, 423–427.

Ditzen, B., Schaer, M., Gabriel, B., Bodenmann, G., Ehlert, U., Heinrichs, M., 2009. Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. Biol. Psychiatry 65, 728–731.

Feldman, R., 2007a. Mother-infant synchrony and the development of moral orientation in childhood and adolescence: direct and indirect mechanisms of developmental continuity. Am. J. Orthopsychiatry 77, 582–597.

Feldman, R., 2007b. Parent–infant synchrony and the construction of shared timing; physiological precursors, developmental outcomes, and risk conditions. J. Child Psychol. Psychiatry 48, 329–354.

Feldman, R., in press. Parent-infant synchrony: A bio-behavioral model of mutual influences in the formation of affiliative bonds. Monographs of the Society for Research in Child Development.

Feldman, R., Eidelman, A.I., 2004. Parent–infant synchrony and the social–emotional development of triplets. Dev. Psychol. 40, 1133–1147.

Feldman, R., Eidelman, A.I., 2007. Maternal postpartum behavior and the emergence of infant–mother and infant–father synchrony in preterm and full-term infants: The role of neonatal vagal tone. Dev. Psychobiol. 49, 290–302.

Feldman, R., Gordon, I., Schneiderman, I., Weisman, O., Zagoory-Sharon, O., 2010. Natural variations in maternal and paternal care are associated with systematic changes in oxytocin following parent–infant contact. Psychoneuroendocrinology.

Feldman, R., Masalha, S., 2010. Parent–child and triadic antecedents of children's social competence: cultural specificity, shared process. Dev. Psychol. 46, 455–467.

Feldman, R., Weller, A., Zagoory-Sharon, O., Levine, A., 2007. Evidence for a xneuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. Psychol. Sci. 18, 965–970.

Fleming, A.S., O'Day, D.H., Kraemer, G.W., 1999. Neurobiology of mother-infant interaction: experience and central nervous system plasticity across development and generations. Neurosci. Biobehav. Rev. 23, 673–685.

Francis, D.D., Champagne, F.C., Meaney, M.J., 2000. Variations in maternal behaviour are associated with differences in oxytocin receptor levels in the rat. J. Neuroendocrinol. 12, 1145–1148.

Francis, D.D., Young, L.J., Meaney, M.J., Insel, T.R., 2002. Naturally occurring differences in maternal care are associated with the expression of oxytocin and vasopressin (V1a) receptors: gender differences. J. Neuroendocrinol. 14, 349–353.

Fries, A.B., Ziegler, T.E., Kurian, J.R., Jacoris, S., Pollak, S.D., 2005. Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior. Proc. Natl. Acad. Sci. U. S. A. 102, 17237–17240.

Gimpl, G., Fahrenholz, F., 2001. The oxytocin receptor system: structure, function, and regulation. Physiol. Rev. 81, 629–683.

Gordon, I., Zagoory-Sharon, O., Leckman, J.F., Feldman, R., 2010. Oxytocin and the development of parenting in humans. Biol. Psychiatry.

Gordon, I., Zagoory-Sharon, O., Schneiderman, I., Leckman, J.F., Weller, A., Feldman, R., 2008. Oxytocin and cortisol in romantically unattached young adults: associations with bonding and psychological distress. Psychophysiology 45, 349–352.

Heim, C., Young, L.J., Newport, D.J., Mletzko, T., Miller, A.H., Nemeroff, C.B., 2009. Lower CSF oxytocin concentrations in women with a history of childhood abuse. Mol. Psychiatry 14, 954–958.

Holt-Lunstad, J., Birmingham, W.A., Light, K.C., 2008. Influence of a "warm touch" support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol. Psychosom. Med. 70, 976–985.

Johnson, M.H., Griffin, R., Csibra, G., Halit, H., Farroni, T., de Haan, M., Tucker, L.A., Baron-Cohen, S., Richards, J.E., 2005. The emergence of the social brain network: evidence from typical and atypical development. Dev. Psychopathol. 17, 599–619.

Keverne, E.B., Curley, J.P., 2004. Vasopressin, oxytocin and social behaviour. Curr. Opin. Neurobiol. 14, 777–783.

Keverne, E.B., Kendrick, K.M., 1992. Oxytocin facilitation of maternal behavior in sheep. Ann. NY Acad. Sci. 652, 83–101.

Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., Gruppe, H., Mattay, V.S., Gallhofer, B., Meyer-Lindenberg, A., 2005. Oxytocin modulates neural circuitry for social cognition and fear in humans. J. Neurosci. 25, 11489–11493.

Kosfeld, M., Heinrichs, M., Zak, P.J., Fischbacher, U., Fehr, E., 2005. Oxytocin increases trust in humans. Nature 435, 673–676.

Lee, H.J., Macbeth, A.H., Pagani, J.H., Young III, W.S., 2009. Oxytocin: the great facilitator of life. Prog. Neurobiol. 88, 127–151.

Levine, A., Zagoory-Sharon, O., Feldman, R., Weller, A., 2007. Oxytocin during pregnancy and early postpartum: individual patterns and maternal-fetal attachment. Peptides 28, 1162–1169.

Light, K.C., Grewen, K.M., Amico, J.A., Boccia, M., Brownley, K.A., Johns, J.M., 2004. Deficits in plasma oxytocin responses and increased negative affect, stress, and blood pressure in mothers with cocaine exposure during pregnancy. Addict. Behav. 29, 1541–1564.

Marshal, P.J., Fox, N.A. (Eds.), 2006. The development of social engagement. Oxford University Press, New York.

Maestripieri, D., Hoffman, C.L., Anderson, G.M., Carter, C.S., Higley, J.D., 2009. Mother-infant interactions in free-ranging rhesus macaques: relationships between physiological and behavioral variables. Physiol. Behav. 96, 613–619.

Meaney, M.J., 2001. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu. Rev. Neurosci. 24, 1161–1192.

Meaney, M.J., 2010. Epigenetics and the biological definition of gene × environment interactions. Child Dev. 81, 41–79.

Naber, F., van Ijzendoorn, M.H., Deschamps, P., van Engeland, H., Bakermans-Kranenburg, M.J., 2010. Intranasal oxytocin increases fathers' observed responsiveness during play with their children: A double-blind within-subject experiment. PNEC, doi:10.1016/j.psyneuen.2010.04.007.

Neumann, I.D., 2008. Brain oxytocin: a key regulator of emotional and social behaviours in both females and males. J. Neuroendocrinol. 20, 858–865.

Pedersen, C.A., 2004. Biological aspects of social bonding and the roots of human violence. Ann. NY Acad. Sci. 1036, 106–127.

Porges, S.W., 2003. Social engagement and attachment: a phylogenetic perspective. Ann. NY Acad. Sci. 1008, 31–47.

Rosenblatt, J.S., 1965. The basis of synchrony in the behavioral interaction between the mother and her offspring in the laboratory rat. In: Foss, B.M. (Ed.), Determinants of infant behavior. Methuen, London, pp. 3 –45.

Ross, H.E., Cole, C.D., Smith, Y., Neumann, I.D., Landgraf, R., Murphy, A.Z., Young, L.J., 2009. Characterization of the oxytocin system regulating affiliative behavior in female prairie voles. Neuroscience 162, 892–903.

Ross, H.E., Young, L.J., 2009. Oxytocin and the neural mechanisms regulating social cognition and affiliative behavior. Front. Neuroendocrinol. 30, 534–547.

Schneirla, T.C., 1946. Problems in the biopsychology of social organization. J. Abnorm. Psychol. 41, 385–402.

Sivakumar, T., Hand, A.R., Mednieks, M., 2009. Secretory proteins in the saliva of children. J Oral Sci. 51, 573–580.

Spielberger, C.D., 1984. State-trait anxiety inventory : a comprehensive bibliography. Consulting Psychologists Press, Palo Alto, CA.

Sroufe, L.A., 2005. Attachment and development: a prospective, longitudinal study from birth to adulthood. Attach. Hum. Dev. 7, 349–367.

Strathearn, L., Fonagy, P., Amico, J., Montague, P.R., 2009. Adult attachment predicts maternal brain and oxytocin response to infant cues. Neuropsychopharmacology 34, 2655–2666.

Weaver, I.C., Cervoni, N., Champagne, F.A., D'Alessio, A.C., Sharma, S., Seckl, J.R., Dymov, S., Szyf, M., Meaney, M.J., 2004. Epigenetic programming by maternal behavior. Nat. Neurosci. 7, 847–854.

Wheeler, W.M., 1928. The social insects. Harcourt, New York.

White-Traut, R., Watanabe, K., Pournajafi-Nazarloo, H., Schwertz, D., Bell, A., Carter, C.S., 2009. Detection of salivary oxytocin levels in lactating women. Dev. Psychobiol. 51, 367–373.
Winslow, J.T., Hearn, E.F., Ferguson, J., Young, L.J., Matzuk, M.M., Insel, T.R., 2000. Infant vocalization, adult aggression, and fear behavior of an oxytocin null mutant mouse. Horm. Behav. 37, 145–155.
Winslow, J.T., Noble, P.L., Lyons, C.K., Sterk, S.M., Insel, T.R., 2003. Rearing effects on cerebrospinal fluid oxytocin concentration and social buffering in rhesus monkeys. Neuropsychopharmacology 28, 910–918.
Wotjak, C.T., Ganster, J., Kohl, G., Holsboer, F., Landgraf, R., Engelmann, M., 1998. Dissociated central and peripheral release of vasopressin, but not oxytocin, in response to repeated swim stress: new insights into the secretory capacities of peptidergic neurons. Neuroscience 85, 1209–1222.
Zak, Kurzban, R.O., Metzner, W.L., 2004. The neurobiology of trust. Ann. NY Acad. Sci. 1032, 224–227.
Zak, Kurzban, R.O., Metzner, W.L., 2005. Oxytocin is associated with human trustworthiness. Horm. Behav. 48, 522–527.