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## Oxytocin: A Parenting Hormone

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### Highlights

- The expression of parenting in both human and non-human mammals is affected by hormones
- Oxytocin provides a neuroendocrine template for the effects of multiple hormones on parenting
- Oxytocin measured across pregnancy and the postpartum explains variance in parenting behavior
- Nasal administration of oxytocin influences neural responses to infant signals such as crying and laughter.
- Childhood experiences and attachment style may moderate the effects of oxytocin administration

### Key Words

parenting, hormones, oxytocin, synchrony, intervention

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## **Abstract**

In non-human mammals mothering is hormone-dependent, with crucial roles for oxytocin and prolactin. While human parenting is not hormone-dependent, hormonal changes in oxytocin, vasopressin, prolactin, testosterone, and cortisol prime and accompany the expression of parenting. In the following we focus on oxytocin (OT) as a key hormone in human parenting. OT is a nine-amino-acid neuropeptide hormones which evolved from the ancient vasotocin molecule approximately 650 MYO. OT is implicated in sociality across vertebrate evolution and substantial research has pinpointed its role in birth, lactation, and maternal care in mammals. Over the last decade, studies have begun to examine peripheral levels of OT – in plasma, saliva, urine, and to lesser extend CSF – in humans as well as OT administration to parents. Correlational and experimental studies indicate that OT is associated with increased parent-child synchrony, sensitive parenting, and parental contact; interacts with other hormones, such as vasopressin, cortisol, or testosterone to create parent-specific effects; is associated with activation of key nodes in the parental brain, and is altered in conditions of high risk or parental psychopathology. We conclude by discussing the potential role of OT in interventions for high-risk parenting.

## Oxytocin: A Parenting Hormone

Mammalian mothering in non-human animals is hormone-dependent. Hormonal changes during pregnancy and parturition causally determine the expression of maternal behavior and experimental manipulations on key hormones alter or eliminate maternal care [1-6]. Studies in rodents described the critical role of oxytocin (OT) and prolactin for the onset of maternal behavior; the contribution of stress hormones, particularly corticosterone, to maternal care [7-9]; and the role of vasopressin and testosterone particularly in the context of fatherhood [10-12]. In combination with sex-related hormones (estradiol, progesterone), these establish the neuroendocrine milieu that enables rodent mothers (and fathers in the 3-5% of mammalian species who are bi-parental) to parent [13-15].

Human parenting is not hormone-dependent; however, hormonal changes prime and accompany the expression of parenting [2, 16-18]. Humans' large associative cortex, neural plasticity, and massive limbic-cortical projections enable bottom-up behavior-based processing, so that committed parental care can trigger the hormones of parenting even without pregnancy and childbirth; for instance in primary-caregiving fathers or adoptive parents [19, 20]. Parenting-related hormones are also linked with multiple neurobiological indices, such as brain activations, allelic variability, and autonomic functioning [21-25]. Evidence suggests that individual variations in OT are meaningfully associated with variations in maternal and paternal behavior and can index disruptions under high-risk conditions, such as premature birth, maternal depression, or contextual risk [1, 26, 27]. Maternal depression across the first years of life [28] has been linked with lower baseline OT [29] and attenuated OT response [30] in both mother and child. Moreover, "endocrine synchrony" between OT levels in parent and child have been demonstrated, highlighting the interactional transfer of parent-child neurobiology [31, 32]. Finally, human studies indicate that parental postpartum OT levels, in combination with parent-infant synchrony, are associated with later child well-being and social outcomes [33], underscoring their usefulness as early indices of adversity. Overall, these studies highlight the importance of understanding the contribution of OT to human parenting and parent-child interaction.

Importantly, hormones other than OT meaningfully contribute to the expression of parental care. Vasopressin, prolactin, testosterone and cortisol have all been associated with various aspects of parenting in mothers and fathers; yet studies have also shown associations between OT and these hormones or their complex combined effects on parenting behavior. Here we present studies, particularly from the past decade, on OT and parenthood, guided by the perspective that the integrative oxytocinergic system provides a template for the integration of multiple hormones in support of human parenthood [34].

### **Animal studies**

There are good reasons to submit that OT has been involved in life-sustaining and reproductive processes throughout animal evolutionary history [21], but rats, sheep, and voles dominate animal OT research.

Nulliparous female rats avoid or attack pups, and show maternal behavior only after parturition, when progesterone levels go down, estradiol levels increase, and the OT production in the hypothalamic paraventricular nucleus and supraoptic nucleus is strongly upregulated. After OT injection, however, virgin females display all essential aspects of maternal behavior, including nest building and assuming a nursing posture [35, 36]. Since olfactory stimuli appear to elicit negative behaviors to pups in virgin rats, OT (linked to the dopaminergic reward system) must play a role in the shift in the valence of pup odors from negative to positive [37].

Olfactory input does also play a role in concert with the oxytocinergic system in sheep. Similar to rats, sheep show maternal behavior only after parturition or, alternatively, with experimentally increased OT levels [38, 39]. A difference between sheep and rats is that postpartum female rats will care for any young, while a postpartum ewe rejects other lambs: she recognizes the specific odor of her own lamb, and develops an enduring and exclusive mother-infant bond with this specific lamb. When the main olfactory bulb is inactivated, ewes do care for any young, also those that are not her own, without forming a selective caregiving relationship.

Voles have become famous because they come in distinct types: Prairie voles are monogamous, nest together, and both parents take care of the young, whereas meadow voles and montane voles breed promiscuously, do not form pair bonds, and parental care is provided by females only. The voles are closely related genetically, and are similar in physical appearance. The difference is explained not by the density of OT receptors, but by different distributions of these receptors. Prairie voles – both males and females – have greater densities of OT receptors in the nucleus accumbens and the basolateral amygdala; montane voles have a greater density of OT receptors in the lateral septum. Similarly, densities of AVP differ between the vole types [37]. Equal levels of the peptides thus regulate behavior differently, illustrating the notion that the neurobiology of parenting is an intricate concerted action of many mechanisms, of which the salivary, plasma or even cerebrospinal fluid OT levels are only weak representations.

Even so, recent animal work has attracted attention for the very reason that increased OT levels in cerebrospinal fluid could be demonstrated after nasal OT administration. Doubts have been raised as to whether a sniff of OT does reach the brain [40, 41], and since taking samples from cerebral spinal fluid (CSF) in healthy human participants for the assessment of OT levels is too intrusive, the animal model is a welcome approach to address this issue [42]. In rats and mice increased brain and plasma OT levels after nasal application were found, both in the hippocampus and in the amygdala, with peak values between 30 and 60 min after administration [43]. Similarly, inhaling increased OT levels in CSF in rhesus monkeys [44]. Although levels in CSF do not translate directly into levels in specific brain tissues, these studies add support to the hypothesis that the nasal anatomy offers several pathways for OT to reach the brain [45]. Behavioral effects attest to this idea, too, as inhaled OT increased positive social behaviors in newborn macaques [46].

## Studies in Humans

*Correlational designs.* OT measured across pregnancy and the postpartum predicted the emergence of the human-specific maternal repertoire, indicating a priming effect [47]. In the first months of life, OT levels in caregiving fathers were no different from mothers and were associated with the parent-specific repertoire; affectionate touch, vocalizations, and gaze in mothers, and high arousal and stimulatory contact in fathers. Mothers who provided more affectionate contact with their infants exhibited OT increase, whereas for fathers it was not so much affectionate contact but high levels of stimulatory contact with their infant that resulted in an OT increase [48]. Moreover, infants as young as 4 months old displayed OT increase following synchronous interactions [31]. Longitudinal studies demonstrate the importance of parental OT functionality not only for the consolidation of children's long-term OT system but also for the development of social competencies. Parental OT combined with parent-infant synchrony predicted preschoolers' OT response and social reciprocity with best friends [33]. Similarly, in a 4-year follow-up parental brain response and OT in infancy predicted preschoolers' OT, emotion regulation, and socialization. Listening to mother's voice during stress elevated children's urinary OT and enabled better stress management [49]. OT levels also correlate with activation of key nodes in the parental brain when parents are exposed to their own infant stimuli [26]. These studies show parallels between OT functioning in humans and other mammals in the context of parenting and attest to the cross-generation transmission of OT in humans as mediated by parental behavior.

*Experimental designs.* In experimental research with intranasal OT administration two types of studies of parenting prevail: studies with actual parenting behavior as outcome, and studies focusing on behavioral or brain responses to infant stimuli in more controlled experimental designs.

The first two within-subject experiments with actual parenting behavior as outcome involved fathers, one group with typically developing toddlers and one group with toddlers in the autism spectrum. Fathers in both groups were significantly more vigorous and stimulating during play in the OT condition [50, 51]. This experimental finding mirrored and corroborated the correlational results that fathers who were more stimulating in their play had higher levels of salivary OT after the play session compared to fathers with less stimulating interactions [48]. In the third study, oxytocin administration increased fathers' touch and father-infant reciprocity [52]. Postnatally depressed mothers did however not benefit from experimentally elevated OT levels in terms of their sensitive interaction [53], nor did it ameliorate their depressive symptomatology, although it did improve their protective behavior toward their infants in the presence of an intrusive stranger [54].

In experimental designs with standardized infant stimuli, OT has been found to affect neural responses in meaningful ways. OT administration reduced amygdala activation and increased insula and inferior frontal gyrus activation in response to infant crying [55], which may prevent anxious or aversive feelings and enhance empathic concern. Moreover, when in a different sample context information accompanied the same infant crying sounds (now labeled as 'sick' or as 'bored'), OT enhanced insula,

inferior frontal gyrus and amygdala responding to sick infant crying but lowered neural reactivity to the very same crying sounds when the infant was labeled as being bored [56]. Oxytocin thus appears to facilitate flexible adaptation of responses to infant crying depending on contextual information.

Importantly, OT may further facilitate parent–infant bonding by increasing the reward value of enjoyable infant signals. OT induced stronger functional connectivity between the amygdala and neural reward centers during exposure to infant laughter [57]. The up-regulation of the rewarding aspects of parenting after OT administration may also be indicated by an increase of activation in the right caudate when fathers viewed pictures of their own infant compared to an unknown infant [58].

Taken together, these studies seem to illustrate a supportive role of OT in the establishment of a secure parent-infant attachment. Unfortunately, however, a number of studies suggest that the positive effects on behavior or neurobiology may be minimal or absent in individuals with negative childhood experiences or insecure attachment styles [59-61]. For example, aggressive behavioral responses to infant crying decreased after OT administration compared to placebo, but only in participants without experiences of harsh parental discipline during childhood. For those who were disciplined harshly in the past no differences between the OT and placebo conditions emerged [62]. This limits the feasibility of OT as a stand-alone pharmacological treatment for those most in need of parenting support. The potential role of such treatment as an augmentative approach combined with supportive parenting intervention programs is in need of further exploration [63].

Figure 1: A research program for the role of oxytocin in parenting and development.

### **Implications for future research and clinical practice**

Our brief review does not do justice to the vast literature on parenting and hormones in general and OT in particular. Yet, despite extant research, there is much we do not know about the neuroendocrine basis of human parenting, and we delineated a research program for the role of oxytocin in parenting and development (Figure 1). There is a need to develop reliable assays for biomarkers that likely play a key role in parenting, such as immune biomarkers, serotonin, or dopamine, preferably from saliva or non-invasive fractions. Longitudinal studies following children from birth and collecting hormones at numerous time-points from parent and child are still rare. The integration of multiple physiological systems, including genes, brain, hormones, autonomic functioning, and careful observations of behavior would provide new perspectives on the way OT and other hormones impact and are impacted by physiological and behavioral processes across development.

Finally, there is a need to refine research on endocrine biomarkers of high-risk parenting. Hormones can provide early markers of disruptions to parenting processes, but much research is still needed to standardize measurements, define curves, and describe optimal versus non-optimal ranges at various ages and across cultural contexts. Further research is needed to fully understand how specific conditions, such as maternal depression, trauma, or personality disorder, translate into OT and other hormonal profiles, what is stable over time and what is transient, and how interventions can modify hormonal levels. Hormones provide a wealth of information on patterns of parental care across infant development in different cultural contexts and childrearing conditions and careful studies are needed to deepen our understanding of their direct and subtle impact on parenting.

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Figure 1

