Bonding is a special connection between individuals. It might be observed between mothers and their babies, lovers, family, friends, or even between owners and their pets. Bonding is a description of feelings that encompasses measurable parameters of attachment to another individual and reward by being attached. These parameters are sometimes used to scientifically define love. In the case of the mother-infant bond, there is recognition of the infant, and desire and action to give warmth, comfort, food, and protection. It has been known for many years that the neuroendocrine hormone, oxytocin, and the monoamine, dopamine, play key roles in initiation and maintenance of such behaviors. The Meaney lab (1) has been instrumental in establishing the separate importance of oxytocin and dopamine in mother-infant interaction and in showing that individual variation in these central systems underlies differences in quality of the behavior. However, exactly how and where oxytocin acts centrally in maternal behavior has been relatively ill defined, partly because oxytocin receptors are widely distributed and partly because oxytocin has multiple simultaneous roles perinatally. Now the precise roles for oxytocin in mediating this dialogue are emerging and dopamine in particular is a promising target.

In the Meaney rat model of “good” mothers (defined as those exhibiting high licking, grooming, and arched-back nursing behavior), high oxytocin receptor expression in key brain regions, such as the medial preoptic area (MPOA), ventral tegmental area (VTA), and nucleus accumbens, is evident (2). Good mothers can even pass on their maternal skills to daughters, and underlying this is epigenetic inheritance of oxytocin receptor expression patterns (3). “Poor” mothers do not show the same receptor patterns, but, when their offspring are cross-fostered to good mothers they can then acquire the beneficial receptor and behavioral patterns (4). On the other hand, when good mothers are stressed, brain oxytocin receptor patterns and maternal behavior are compromised (4). The important role of oxytocin is reinforced by insightful studies showing oxytocin-mediated intense functional magnetic resonance imaging (fMRI) signals in the VTA and nucleus accumbens during suckling (5). Similar studies have been conducted also in women, where feelings of maternal love are associated with intense fMRI activation of the same brain regions in response to viewing pictures of their babies (6).

Although oxytocin receptor patterns underlie oxytocin action, the effects of dopamine depend on its release. For example, increased dopamine in the nucleus accumbens equates with quality of maternal behavior (7). Transgenic mice lacking dopamine transporter exhibit impaired maternal behavior (8, 9). The sources of dopamine facilitating maternal behavior are the VTA and the substantia nigra, and lesions using 6-hydroxydopamine to selectively destroy monoamine cells block maternal behavior (10). Champagne et al. (7) developed the powerful technique of voltammetry to measure dopamine release in conscious rats, and elegantly showed that minute-by-minute dopamine release in the nucleus accumbens correlates with licking and grooming behavior. One of the most interesting findings of the Bartels and Zeki paper (6) is that the oxytocin receptor-rich regions that are shown to be activated by fMRI overlap to a great extent with dopamine source and target regions, including the nucleus accumbens. In this issue of Endocrinology, Shahrokh et al. (11) have now estab...
lished a strong functional link between the oxytocin projections and dopamine neurons in nursing mother rats, and this is dependent on whether they are good mothers or not.

Although it had already been proposed that oxytocin released in the brain after birth modulates dopamine activity in dopamine source and target regions like the nucleus accumbens, VTA, and substantia nigra (10), and that oxytocin antagonist microinjection into the VTA impairs maternal behavior (12), the precise nature of the oxytocin-dopamine interaction during exhibition of licking and grooming behavior was unclear. Shahrokh et al. (11) now clearly demonstrate that individual differences in oxytocin expression, targeting, and associated dopamine release underlie individual differences in behavior. This is of interest because both oxytocin and dopamine neurons are responsive to environmental conditions, like stress, and might become compromised in the mother’s brain before, during, or after pregnancy (Baskerville T.A., and A.J. Douglas, submitted for publication). This could obviously then impact on her ability to provide optimal care for the offspring. The study reveals, using sophisticated in vivo techniques, that oxytocin action within the VTA in the high licking and grooming mothers underlies dopamine release within the nucleus accumbens, specifically locating oxytocin action to this dopamine source and powerfully revealing the importance of the oxytocin-dopamine interaction located in the mesolimbic pathway. Last, but not least, the study shows high oxytocin expression and increased direct projections of oxytocin neurons from the MPOA and paraventricular nucleus (PVN) to the VTA in good mothers, importantly suggesting the involvement of parvocellular oxytocin neurons in the bonding-related behaviors.

This identification of parvocellular oxytocin neuron function is valuable because in some cases the source of oxytocin that mediates nucleus accumbens function during bonding has been unknown (Baskerville T.A., and A.J. Douglas, submitted for publication). Furthermore, it has been speculated that oxytocin could diffuse from hypothalamic sources to drive behaviors and the large amount of oxytocin released from magnocellular neuron dendrites makes this feasible (13). Oxytocin diffusing centrally can then act on its suite of widely distributed receptors to control different behaviors simultaneously. Therefore, although this paper gives evidence supporting terminal release of oxytocin in the VTA that underlies dopamine release in the nucleus accumbens, an additional role for dendritically released oxytocin in the nucleus accumbens should not be ruled out entirely. Oxytocin receptor patterns rather than specific release sites are also implicated in social and partner bonding, as shown in the prairie vole model (14).

In fact, an oxytocin-dopamine interaction is suggested to underlie partner preference and parental behavior in prairie voles (Baskerville T.A., and A.J. Douglas, submitted for publication; and Ref. 14) and, like the maternal imaging study in humans discussed above, fMRI also reveals potential interaction between oxytocin and dopamine in association with feelings of romantic love (6). Oxytocin release increases in the nucleus accumbens in female voles during pairing (15), although the source of oxytocin was not reported, and coactivation of dopamine and oxytocin in the nucleus accumbens facilitates pair bonding in female prairie voles (16). In the light of the current study, it may be that oxytocin release in the VTA drives the dopaminergic component of pair bonding.

Interestingly, inputs to the PVN from the incertohypothalamic dopamine neuron populations (A13/14/15) impinge on and activate oxytocin neurons and neurons in the MPOA correlated with maternal behavior (17). Oxytocin neurons express a range of dopamine receptors, particularly the D2-like receptors comprising D2, D3, and D4 receptors (17), so potentially respond directly to dopamine drive. It may be that the physical stimuli associated with close contact, including licking and grooming the baby and sucking the nipple by the baby stimulates these excitatory dopamine pathways that recruit hypothalamic oxytocin neurons. Then, as part of their suite of actions, oxytocin neurons stimulate the mesolimbic dopamine pathways associated with motivation and reward for attachment. Therefore, there is likely to be a reciprocal in-

![Diagram](https://example.com/fig1.png)

**FIG. 1.** Interaction between oxytocin and dopamine in maternal-infant bonding. Dopamine neurons in the zona incerta (ZI) and VTA project to oxytocin somata in the PVN and MPOA, and vice versa. Parvocellular oxytocin terminals in the VTA and nucleus accumbens (NAc) induce release and/or activation of dopamine and reciprocally, dopamine terminals activate oxytocin neurons. This interaction is evidently key to many mother-infant bonding behaviors. A role for dendritically released oxytocin [e.g. from the magnocellular PVN and supraoptic nucleus (SON)] that diffused to the NAc in driving dopamine effects is also likely.
teraction between dopamine-oxytocin and oxytocin-dopamine in these socially based behaviors that together underlie what we understand as bonding, or love (Baskerville T.A., and A.J. Douglas, submitted for publication and Fig. 1).

Acknowledgments

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