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Commentary

Variations in Maternal Behavior—Oxytocin and Reward Pathways—Peripheral Measures Matter?!

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There is a growing body of evidence from animal studies that centrally released oxytocin (OT) from hypothalamic nuclei is one component of a complex bio-behavioral system that is crucial for the emergence of mother–infant bonding (Ross and Young, 2009). Variations in limbic circuitry involving the nucleus accumbens and amygdala nuclei, and interactions with central OT and dopamine systems have also been associated with individual differences in maternal behavior in rodents. For example, Shahrokh *et al* (2010) found that in rat dams, stable, individual differences in pup licking/grooming were abolished by OT receptor blockade and that this effect was mediated by the direct effect of OT on dopamine release within the mesocorticolimbic dopamine system. While animal models of maternal behavior are compelling and have identified key regions in a putative mothering circuit, it is also clear that human behaviors are far more complex. Processes such as cognitive flexibility, attentional control, working memory, and the mother's ability to understand the intentions and emotions of her child are fundamental components of human mothering (Barrett and Fleming, 2011).

In this issue of *Neuropsychopharmacology*, Atzil *et al* (2011) performed functional magnetic resonance imaging (fMRI) to assess the neural circuitry of new mothers when their infants were 4–6 months old. The fMRIs were recorded while mothers viewed a 2-min movie of their own infant during solitary play and a 2-min movie of themselves during the mother–infant interaction *vs* a 2-min movie of an unfamiliar infant and segments of mother–infant interactions. The methods used in this study are state-of-the-art and include (1) the micro-coding of actual mother–infant dyadic interactions; (2) the use of videotapes of these dyadic interactions as one of the stimuli used in the fMRI study; and (3) the measurement of peripheral levels of OT. Their findings are noteworthy and represent a substantial incremental step forward. The most notable findings include a significant correlation of ratings of maternal 'synchrony', where there is a close coordination of maternal and infant behavior (gaze, vocalizations, affectionate touch, and positive affect) based on the objective micro-coding of the mother–infant dyadic interactions with peripheral OT levels. In addition, they observed differential patterns of activation in the left nucleus accumbens and right amygdala, as well as differential patterns of interconnectivity in mothers with high levels of synchrony *vs* mothers with high levels of 'intrusiveness' characterized by mothers providing stimulatory or proprioceptive touch, or presenting objects when infants showed gaze aversion and a need for rest.

This study joins two other reports that together directly link the OT system in new mothers with the brain reward and limbic neural circuits (Strathearn *et al*, 2009; Riem *et al*, 2011). Strathearn *et al* (2009) found that mothers with secure attachment viewing their own infant's smiling and crying faces during fMRI scanning showed greater activation of the ventral striatum and the OT-associated hypothalamus/pituitary region. In addition, the change in plasma OT following an episode of physical interaction with their infant was directly correlated with greater activation of the hypothalamus/pituitary region in response to their own *vs* an unknown infant's face (happy, sad, and neutral). In contrast, Riem *et al* (2011) performed a randomized-controlled trial to examine the influence of intranasally administered OT on neural responses to infant crying. Intranasal OT significantly reduced activation in the right amygdala and increased activation in other limbic and frontal regions.

The clinical implications of these studies are yet to be fully explored. However, the observation by Skrundz *et al* (2011) that expectant mothers at risk for postpartum depression have lower levels of plasma OT during pregnancy re-enforces the possibility that behavioral and/or biological interventions that would enhance the release of OT during pregnancy could contribute to the prevention of postpartum depression, and its immediate and long-term developmental consequences for both the mother and the child. Similar questions are currently being asked with regard to other early-onset neuropsychiatric disorders, including autism spectrum disorders (Bartz *et al*, 2011).

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Beyond these clinical implications, questions abound in this area of research. We, along with other investigators, remain intrigued by how the peripheral and central OT systems interact moment-to-moment over the course of development to influence social relationships (for a review, see Gordon *et al*, 2011). To date, individual stability in peripheral OT levels has been reported in adults over the course of several months, but can it be observed over several years and across developmental transitions? What about the infant's level of peripheral OT? Is it stable, and how much does it depend on the attachment style and dyadic interactions with caregivers? Beyond pregnancy and infancy, how does the OT system function during periods of rapid brain reorganization (eg, puberty) *vs* those of relative developmental stability? Is the source of OT being measured in the plasma and saliva entirely derived from the posterior pituitary, or do somatic sources including the heart, thymus, GI tract, testis, and ovaries contribute? If peripheral sources do contribute, what regulatory mechanisms guide this process and do they differ depending on gender, age or social context? What role do sensory afferents and the autonomic nervous system play as we seek to understand the brain–body interface and the role of OT in social motivation within dyadic relationships?

Finally, we are curious about how variable the distribution and density of OT receptors is in humans, and how individual differences vary depending on gender, developmental stage, and the initiation of intimate dyadic relationships. To what extent are central or peripheral OT receptors sensitive to epigenetic modification and to what extent do they contribute to patterns of parental care that can be passed on in a quasi-Lamarckian fashion from generation to generation are closely related questions.

Although OT is a key element in this unfolding story, it is surely not the only one. Moving forward, we must continue to examine the relationships between OT and other components in our highly complex biological and emotional worlds, and how they produce the rich and highly nuanced, dynamic interpersonal relationships that are characteristic of our species.

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