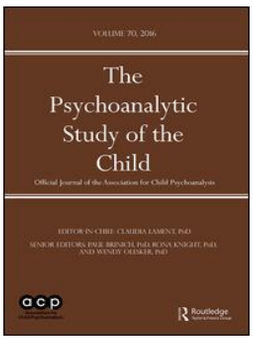

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Trauma, Mothering, and Intergenerational Transmission: A Synthesis of Behavioral and Oxytocin Research

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ABSTRACT

Although intergenerational effects of traumatic experiences have garnered increased clinical and empirical attention, not much is known about the mechanisms by which trauma-related distress is transmitted. This paper brings together insights from mother–infant attachment research and oxytocin research to provide a neurobiobehavioral account of how maternal trauma affects the mother, the mother–infant attachment, and the infant. We draw from both behavioral and oxytocin research to shed light on how the cycle of intergenerational transmission is perpetuated and to consider what can be done to disrupt the cycle. We conclude by pointing toward a strategy for intervening in the intergenerational transmission of trauma, highlighting areas where further research is needed.

KEYWORDS

Attachment; intergenerational transmission; oxytocin; unresolved trauma

Four decades ago, the now well-known metaphor "ghosts in the nursery" (Fraiberg, Adelson, and Shapiro 1975) was coined, vividly capturing the hypothesis that the mother's past trauma—if not accessed, processed, and resolved—will "intrude into" the mother–infant relationship, repeating the tragedies in the dyad. This evocative description anticipated a complex but solid body of literature on the intergenerational repetition of traumatic experience (Madigan, Bakermans-Kranenburg, et al. 2006; Lieberman et al. 2011; Bowers and Yehuda 2016). Maternal trauma history, or more precisely its psychobiological effects, generates vulnerability in the child, which translates into increased likelihood of traumatic parenting on the part of the maltreated child, now fully grown. This phenomenon is most clearly seen in dramatically high rates of child abuse inflicted at the hands of mothers who were themselves once abused (Dixon, Hamilton-Giachritsis, and Browne 2005; Lieberman et al. 2011). A decade of close empirical scrutiny has shown comparable, albeit more subtle, findings in the homes of traumatized but nonmaltreating mothers: traumatized mothers, even nonmaltreating ones, have been shown to beget frightened children. This comes from a long line of prospective longitudinal and cross-sectional studies (Hesse and Main 1999; Lyons-Ruth and Block 1996) of mother–infant dyads that have repeatedly noted infants' frightened

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and alarmed behaviors (e.g., immobilized behavior and dazed appearance) while in the presence of their traumatized mothers.

During the past decade, studies have expanded from behavioral (Madigan, Bakermans-Kranenburg, et al. 2006) to neurobiological (Kim, Fonagy, Allen, and Strathearn 2014), genetic (Bokhorst et al. 2003; Fearon et al. 2006), and epigenetic levels (Van Ijzendoorn and Bakermans-Kranenburg 2006; Yehuda and Bierer 2008) in search of the correlates of and contributors to the observed intergenerational transmission. To this day, central questions remain of critical interest to researchers and clinicians alike. How does maternal trauma modify caregiving and how does this altered caregiving disrupt the normative development of children? What does research reveal about bringing the intergenerational pattern to a halt? What steps can be taken to help these mothers break the cycle and protect them from becoming their own mothers, as they themselves often fear?

In this paper, we review the data that are currently available to address the foregoing questions. In doing so, we highlight the possible role of the oxytocin (OT) system in mediating this intergenerational transmission of trauma. The OT system has emerged as a key system contributing to social affiliation and bond formation in a number of species, and has received extensive attention over the past few decades from the scientific community and the general public for its role in both maternal behavior and regulation of stress and fear (Campbell 2010; Meyer-Lindenberg et al. 2011). In the following sections, we first define and conceptualize maternal trauma. Second, we provide an overview of the OT system. Third, we examine how maternal trauma could affect the mother, mother–infant attachment, and the infant. We do so by first summarizing recent advances in the mother–infant behavioral literature before discussing corresponding neurobiology in the respective literature on OT. Finally, we conclude by synthesizing this literature with regard to disrupting the cycle of intergenerational transmission, suggesting clinical interventions and pointing to new avenues for research.

Maternal trauma

This paper focuses on attachment trauma, the kind of trauma that takes place in the context of attachment relationships and undermines one's capacity to develop and maintain future attachment relationships. At its core, trauma thwarts the very core functions of attachment relationships, *secure base* and *safe haven* (Bowlby [1969] 1982), and thereby weakens the early and most basic foundation of emotion regulation (Fonagy and Target 1997). Attachment trauma in this sense is not limited to assaults and violence that are often associated with posttraumatic stress disorder (PTSD), but also encompasses more covert forms, including disrupted relationships and insecure attachment (Lyons-Ruth and Jacobvitz 2008; Allen 2013). These dysregulating experiences in attachment relationships (e.g., chronic misattunement, prolonged separation) are relatively subtle, but are repetitive and sustained. Therefore, although their effects are often less dramatic than those of overt forms of trauma, these effects are nevertheless profound, potentially lifelong, and even transgenerational (Lyons-Ruth and Jacobvitz 2008; Baradon 2010; Solomon and George 2011).

In this paper, we review our current state of understanding of maternal trauma using the construct of *unresolved trauma*.[1] Although we do consider relevant PTSD literature, we rely heavily on the construct of unresolved trauma for three reasons. First, as shown later, the construct first emerged in the field of attachment and is hence well-suited to

capturing trauma that unfolds in the context of attachment. Second, as such, it is particularly useful in considering intergenerational effects associated with trauma. Third, the construct does not limit itself to observable trauma-related symptomatology, but rather encompasses it, while tapping into underlying experiences that might mediate overt disturbances in the mother's functioning, including those that manifest in the mother–infant relationship. We now turn to a review of the OT system.

Oxytocin affiliation system

The neuropeptide hormone OT is synthesized in the paraventricular (PVN) and supraoptic nuclei of the hypothalamus and released into the periphery from the posterior pituitary gland (Gimpl and Fahrenholz 2001). Well-known functions of OT, such as uterine contraction during labor and milk ejection during lactation, arise from the peptide's peripheral actions. Within the central nervous system, OT neurons project between brain regions known to be critical for the expression of attachment behavior, including the medial preoptic area (MPOA), bed nucleus of the stria terminalis (BNST), ventral tegmental area (VTA), ventral striatum (VS), and amygdala (AMY; Francis, Champagne, and Meaney 2000; Numan 2006). Today considerable attention surrounds OT's central actions, including its role in the regulation of attachment and other social functions (Meyer-Lindenberg et al. 2011; Feldman 2012; Benarroch 2013). Before examining the role of OT in trauma and its intergenerational transmission, we underscore next three central actions of OT: its regulation of social behavior, maternal behavior, and stress and fear-related behavior.

Oxytocin and social behavior

OT, the so-called social neuropeptide, is a key neuroregulator of social behavior across mammalian species (Campbell 2010; Meyer-Lindenberg et al. 2011). Popularly referred to as "the hormone of love" (Newton 1973), OT is involved in bond formation (Schneiderman et al. 2012; Love 2014) and many critical aspects of social cognition (Young 2015), including emotion recognition (Lischke et al. 2012; Perry et al. 2013), empathy (Gonzalez-Liencres, Shamay-Tsoory, and Brune 2013), and trust (Van IJzendoorn and Bakermans-Kranenburg 2012). The role of OT in maternal behavior is examined separately in the next section, but here we briefly discuss the role of OT in broader social and affiliative functions.

Injection of OT into the cerebrospinal fluid of sheep induces maternal-like behavior toward unfamiliar lambs, even in nonparent ewes (Kendrick, Keverne, and Baldwin 1987). In vole species, OT-rich areas of the brain (e.g., VS) show an increased density of OT receptors in highly social species compared to species that are less social (e.g., prairie vole, *M. ochrogaster* vs. montane vole, *M. montanus*, respectively). Blocking OT receptors eliminates affiliative behavior in prairie voles, whereas OT treatment facilitates mating (Williams et al. 1994; Young et al. 2001). Studies using OT-related mutant mice have been instrumental in further delineating the role of OT in social processing. Transgenic mice without the OT gene (and hence lacking OT production) display profound deficits in social recognition (Ferguson et al. 2000; Choleris et al. 2003), which are reversed by intraventricular injection of OT (Ferguson et al. 2001). Similar patterns are observed in mice mutant for the CD38 gene, a gene responsible for OT secretion in the hypothalamus (Jin et al., 2007).

In humans, studies have either assessed peripheral levels of endogenous OT or used intranasally administered exogenous OT to examine the nature of the link between OT and social functions. Peripheral OT levels have been associated with temperamental and affective sensitivity (Strathearn et al. 2012), relational reciprocity (Schneiderman et al. 2012), trust and trustworthiness (Zak, Kurzban, and Matzner 2005), and perceived levels of partner support (Grewen et al. 2005). Intranasal administration of OT has been shown to enhance positive communication in relationships (Ditzen et al. 2009), improve efficiency in recognizing and processing of socioemotional cues (Domes et al. 2007; Guastella, Mitchell, and Mathews 2008; Guastella et al. 2009), and increase trust behavior and generosity in money transferring games (Kosfeld et al. 2005; Zak, Stanton, and Ahmadi 2007). Intranasal OT administration has further been shown to effectively reduce socioemotional deficits in individuals with known dysfunction of social cognition, including autism spectrum disorder and schizophrenia (Hollander et al. 2007; Feifel, Shilling, and MacDonald 2016; Yatawara et al. 2016).

Oxytocin and maternal behavior

Of all social bonds, the bond between the mother and infant has the strongest and most well-documented ties to OT. In coordination with estrogen and progesterone, OT helps to facilitate the mother's neurobiological adaptation during the pre- and postpartum period (Rilling and Young 2014). Estrogen and progesterone levels increase steadily during pregnancy until a precipitous drop is observed in progesterone shortly preceding parturition (Brunton and Russell 2010). In preparation for this imminent event, the maternal brain increases OT receptor expression, thus maximizing its sensitivity to OT production (Numan and Woodside 2010; Rilling and Young 2014). The MPOA of the hypothalamus, a region with abundant OT receptors (Champagne et al. 2001), senses changes in hormonal levels throughout pregnancy and stimulates the onset of maternal behavior at parturition via interaction with the mesolimbic dopamine (DA) circuitry, including the VTA and VS (Stolzenberg and Numan 2011; Rilling and Young 2014).

OT's central role in the onset and maintenance of maternal behavior has been widely documented in rodents. Intraventricular injection of OT stimulates a wide range of maternal behaviors in virgin rats, which normally display aversive behavior toward rat pups (Pedersen et al. 1982). On the other hand, administration of an OT antagonist into the VTA blocks the expression of maternal behavior in rat mothers (Pedersen et al. 1994). OT knockout mice (Ragnauth et al. 2005) and transgenic mice with reduced OT neurons in the PVN (Li et al. 1999) display impaired maternal behavior. The density of OT receptors in the AMY and BNST has been associated with the quality of maternal care observed in rats (Francis, Champagne, and Meaney 2000).

In humans, pregnant and parturient women display higher peripheral OT levels than nonpregnant women (Feldman 2012). Postpartum interactions with their infants further stimulate OT release in mothers (Feldman, Gordon, Schneiderman, et al. 2010; Feldman, Gordon, and Zagoory-Sharon 2010). Over the course of pregnancy and the postpartum period, OT levels show high intraindividual stability but high interindividual variability (Feldman et al. 2007; Levine et al. 2007; Gordon et al. 2010), suggesting that they might constitute a trait-like characteristic that underlies the expression of maternal behavior (Strathearn et al. 2012). Indeed, maternal OT levels have been systematically associated with naturally occurring variations in the quality of observed maternal behavior, such that

mothers with impaired caregiving demonstrate blunted OT functions (Feldman, Gordon, Schneiderman, et al. 2010; Kim, Fonagy, Koos, et al. 2014).

Oxytocin and stress/fear-related behavior

In addition to its role in social and maternal behavior, considerable attention has been directed toward OT's anti-stress and anti-anxiety properties. OT is released in response to stress- or fear-inducing stimuli (Neumann et al. 2000) and serves to modulate stress-induced physiological and emotional responsiveness. Endogenous stimulation of OT dampens the activity of the hypothalamic–pituitary–adrenal (HPA) axis in rodents, as reflected in decreased freezing behavior (Knobloch et al. 2012) and reduced plasma levels of adrenocorticotropic hormone (ACTH) and corticosterone[2] (Heinrichs, von Dawans, and Domes 2009; Neumann 2002). OT-deficient transgenic mice display increased anxiety and elevated levels of corticosterone (Amico et al. 2004), whereas injection of OT attenuates anxiety and fear response (Missig et al. 2010; Slattery and Neumann 2010).

Similarly, in humans, increased OT following breastfeeding has been associated with attenuated HPA axis responsiveness and reduced plasma levels of ACTH and cortisol (Heinrichs, Neumann, and Ehlert 2002). Other forms of endogenous OT stimulation (e.g., via warm touch or massage) have been similarly observed to lower anxiety response and sympathetic nervous system activity (Turner et al. 1999; Holt-Lunstad, Birmingham, and Light 2008). A growing number of studies have used intranasal OT to show that OT reduces levels of self-reported anxiety, cortisol, and AMY reactivity to fearful stimuli (Heinrichs et al. 2003; Kirsch et al. 2005; Domes et al. 2010). Although studies have been extended to patients demonstrating clinical symptoms of anxiety (e.g., social anxiety, obsessive–compulsive disorder, PTSD), the data collected to date are inconclusive regarding the promise of intranasal OT in ameliorating clinically elevated levels of anxiety or stress (Macdonald and Macdonald 2010). We return to this topic in the final section of this paper.

Trauma and the mother[3]

Behavioral

The construct of unresolved trauma has provided a unique conceptual framework from which to empirically examine the "ghosts in the nursery" described by Fraiberg, Adelson, and Shapiro (1975). The classification of unresolved trauma is derived from the Adult Attachment Interview (AAI; George, Kaplan, and Main 1985), a semistructured interview consisting of a series of questions designed to elicit attachment-related autobiographical memories. During discussions of trauma or loss, an individual with unresolved trauma exhibits relatively subtle and transient signs of absorption in past trauma (Hesse and van Ijzendoorn 1999) indicated by linguistic breakdowns (e.g., sudden slips or lapses of grammar). These disturbances in speech are thought to reflect momentary collapses in discourse strategy due to activation of and interference from traumatic information that is avoided and kept segregated under usual circumstances (Hesse and Main 1999; Fearon and Mansell 2001; Crittenden and Landini 2011). As such, unresolved trauma classification provides an index of the extent to which past trauma exerts an ongoing influence on present socioemotional experiences (Fearon and Mansell 2001; Crittenden and Landini 2011).

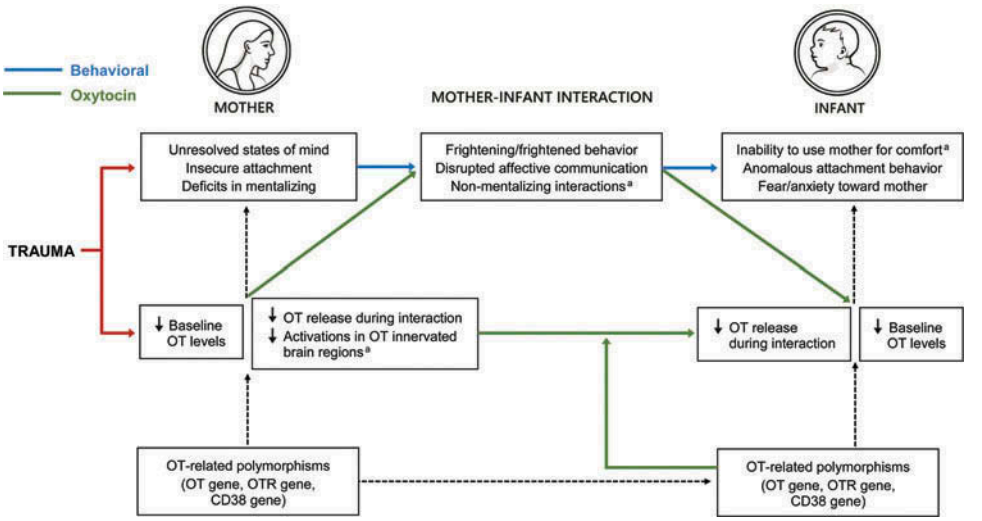

Figure 1. Proposed behavioral and oxytocin pathways involved in the intergenerational transmission of trauma. Adapted from "Mind in the Making: Developmental and Neurobiological Origins of Mentalizing," by S. Kim, 2015, Personality Disorders: Theory, Research, and Treatment, 6, p. 360. Copyright 2015 by the American Psychological Association. OT = oxytocin; OTR = oxytocin receptor; CD38 = a transmembrane glycoprotein critical for the regulation of oxytocin secretion. a These features become more pronounced during moments of infant distress.

Mothers with unresolved trauma are far more likely to have insecure attachment history than secure attachment history (Bailey, Moran, and Pederson 2007; Iyengar et al. 2014). Not surprisingly, the rate of unresolved trauma classification rises in high-risk samples who report a history of childhood abuse (Bailey, Moran, and Pederson 2007; Stovall-McClough and Cloitre 2006), but it is also notably present in low-risk samples with a history of more subtle attachment disturbances (van IJzendoorn and Bakermans-Kranenburg 1996; Bakermans-Kranenburg and van IJzendoorn 2009). A closely related line of work has underscored mentalizing deficits in these mothers, both globally (Fonagy et al. 2002; Slade et al. 2005) and more specifically with regard to trauma (Ensink et al. 2014). To mentalize means to make sense of what unfolds in one's own mind and the minds of others (Fonagy 1991). To mentalize with regard to trauma, then, means to make sense of the mental states (e.g., intentions, feelings, and needs) of the suboptimal caregiver as well as of oneself on both ends of the traumatic experience. Fundamentally, unresolved states of mind reflect deficits in mentalizing. In these unresolved states of mind, traumatic autobiographical information is avoided and segregated rather than processed and integrated. This could serve a self-protective function in the short term, by buffering one from the anxiety of having to come to terms with unwanted information (Fonagy et al. 2002). However, this might also tend to make one more susceptible to the long-term sequelae of trauma, including those outlined in this paper.

Associations between trauma-related symptoms and unresolved trauma have been well demonstrated. Unresolved trauma is consistently reported to be a risk factor for PTSD (Bakermans-Kranenburg and van IJzendoorn, 2009; Stovall-McClough and Cloitre 2006), particularly when both unresolved state of mind and PTSD are assessed with regard to the

same trauma. However, unresolved state of mind regarding an earlier trauma can also increase the risk of later PTSD for an unrelated trauma (Nye et al. 2008; Harari et al. 2009). What has been termed *complex PTSD* (van der Kolk 2002) involves a constellation of symptoms (e.g., dissociation, identity confusion, relational disturbance, affective instability) that are often associated with early and prolonged interpersonal trauma. Compared to traditional symptoms of PTSD (i.e., reexperiencing and avoidance), the symptoms of complex PTSD, and particularly relational/attachment disturbance, demonstrate even stronger links to unresolved trauma (Bailey et al. 2007).

Oxytocin

A history of childhood trauma or stress is consistently negatively correlated with endogenous levels of OT as measured in cerebrospinal fluid, plasma, or urine (Wismer Fries et al. 2005; Heim et al. 2009; Opacka-Juffry and Mohiyeddini 2012; Bertsch et al. 2013). Among different types of trauma, the strongest effects are found for childhood emotional abuse and neglect (Heim et al. 2009; Bertsch et al. 2013). Several studies report a dose-dependent relationship whereby OT concentrations decrease with increased number of trauma exposures (Heim et al. 2009; Opacka-Juffry and Mohiyeddini 2012). The timing of trauma or stress is also important as similar experiences in childhood, but not in adolescence or adulthood, predict OT concentrations in adulthood (Opacka-Juffry and Mohiyeddini 2012). History of insecure attachment has also been linked to adulthood OT functions. Two groups have independently reported reduced levels of OT in insecurely attached adults compared to their securely attached counterparts (Strathearn et al. 2009; Pierrehumbert et al. 2012). Although the link between OT and our construct of interest, unresolved trauma, has yet to be examined, these findings together suggest that trauma or suboptimal early attachment experience might downregulate the functions of the OT system, thereby generating vulnerability to the long-term socioemotional sequelae of trauma, including disturbances in interpersonal relatedness or stress-related symptomatology.

A handful of reports exist concerning overt trauma-related symptomatology (e.g., PTSD) in adulthood and concurrent OT functions. Adulthood trauma-related symptoms appear to be less of a robust predictor of adulthood OT concentrations. One study has provided support for reduced levels of OT in male PTSD patients (Frijling et al. 2015); however, the association did not hold in females and others failed to document the relationship (Heim et al. 2009; Seng et al. 2013; Eidelman-Rothman et al. 2015).

Maternal trauma and maternal behavior

Behavior

Child maltreatment is one of the most extreme manifestations of traumatic parenting among traumatized mothers. The adverse consequences of child maltreatment are evident. The mother is frightening to the child and the child becomes fearful of the very person that he or she is hard-wired to turn to in times of distress. However, a process that is much more subtle than blatant maltreatment displayed by the mother can also lead to interactions that are frightening for the infant. Main and Hesse (1990) were the first to describe that not only frightening but also frightened behavior

displayed by a mother with unresolved trauma can significantly disrupt the mother–infant interaction and evoke fear in the infant. The frightened mother with unresolved trauma might sporadically display dissociative or anomalous behavior (e.g., freezing behavior, altered tone, turning to the infant for comfort when alarmed), which can dysregulate and frighten her infant, who turns to her for comfort. The same process that gives rise to the mother's tendency to exhibit transient signs of absorption in trauma in the AAI are thought to contribute to sporadic lapses during the mother's interactions with her infant, leading her to demonstrate frightening behaviors, frightened behaviors, or both.

Lyons-Ruth, Bronfman, and Parsons (1999) extended this line of work to demonstrate that a much broader range of insensitive and misattuned maternal behaviors that fail to meet the infant's needs can be frightening to the infant. Several types of misattuned maternal behavior were identified and termed disrupted maternal affective communication: (1) affective errors (e.g., offering contradictory cues to the infant, such as inviting him to approach and then distancing from him), (2) disorientation (e.g., displaying frightened affect or sudden loss of affect), (3) negative-intrusive behavior (e.g., mocking or pulling the infant), (4) role confusion (e.g., inducing reassurance from the infant), and (5) withdrawal (e.g., not greeting the infant on reunion). These categories of disrupted maternal affective communication have been shown to be positively associated with the mother's unresolved state of mind with regard to trauma (Goldberg et al. 2003) and negatively associated with the mother's capacity to mentalize her infant's internal states (Grienenberger, Kelly, and Slade 2005). Mothers with unresolved trauma, who tend to be poor mentalizers of their own internal states, tend to also be poor at mentalizing their infant's internal states, leaving them susceptible to impaired mentalizing interactions (Kim 2015), including the disrupted affective communications described earlier.

Beebe et al. (2010) took this line of work even further and underscored that the mother's disrupted attunement is particularly frightening to the infant when it occurs during moments of infant distress. Honing in on the mother–infant interaction on a micro-level through second-by-second analysis, Beebe et al. identified that the aspect of maternal behavior that most severely compromised the infant's subsequent attachment was the mother's failure to attend to her infant's distress, rather than her overall failure of attunement. This work provides a fine-tuned understanding of the essence of traumatic parenting. The infant needs the mother the most in times of distress (Bowlby [1969] 1982). However, when the mother is unable to sense, recognize, and soothe her infant in distress, but rather disengages from the distressed infant, potentially due to dysregulating memories of her own trauma, the infant is left alone in emotional pain that goes unrecognized and unmitigated, and is therefore prolonged. This has the potential to be traumatic for the infant, as trauma is understood to result from intense emotional distress experienced in psychological isolation, which renders the distress unrelieved and protracted (Allen 2013).

Oxytocin

Although no study to date has directly examined the mother's OT functions in relation to her frightening or frightened behavior (Main and Hesse 1990), disrupted affective communication (Lyons-Ruth, Bronfman, and Parsons 1999), or impaired mentalizing communication (Kim,

Fonagy, Allen, Martinez, et al. 2014), there exists a solid body of research documenting that natural variations in maternal OT systematically predict differences in the quality of maternal care. This line of work was first pioneered in rodents by Meaney (2001) and Champagne (2008), who demonstrated that rat mothers who are responsive to their pups show high levels of OT production and high OT receptor densities in brain regions critical for maternal behavior (the MPOA and PVN of the hypothalamus, BNST, AMY, and lateral septum; Francis, Champagne, and Meaney 2000; Champagne et al., 2001). The past decade has seen an extension of this line of work to humans. Compared to mothers who display compromised maternal behaviors, mothers who demonstrate affectionate, sensitive, and synchronous behavior toward their infants show a notable rise in OT levels over the course of pregnancy (Levine et al. 2007), increased baseline OT levels during the postpartum period (Gordon et al. 2010; Atzil, Hendler, and Feldman 2011), and increased OT release during interaction with their infants (Feldman, Gordon, Schneiderman, et al. 2010). These enhanced peripheral OT functions have, in turn, been linked to increased activations of the OT- and DA-innervated brain regions implicated in affiliation and reward, respectively (Atzil, Hendler, and Feldman 2011; Strathearn et al. 2009). The presence of low-risk alleles in the mother's OT-related genes (OT receptor gene, OT gene, and CD38 gene, which regulates OT release) has also been associated with enhanced maternal OT functions and sensitive mothering (Bakermans-Kranenburg and van Ijzendoorn 2008; Feldman et al. 2013; Mileva-Seitz et al. 2013).

There is emerging evidence that the association between maternal OT functions and maternal behavior grows even stronger when examining periods during which the infant is distressed. Mothers with compromised OT functioning show a tendency to shift their gaze away from their infant more frequently and direct their gaze toward their infant less. This pattern is less prominent during moments of infant non-distress but becomes particularly pronounced when the infant is distressed (Kim, Fonagy, Koos, et al. 2014). Although no studies have yet examined the links among maternal trauma, OT, and maternal behavior, the behaviors of mothers with compromised OT bear striking resemblance to the traumatic mothering documented by Beebe et al. (2010): both of these groups of mothers look away and disengage from their infant when the infant is distressed. A recent functional magnetic resonance imaging (fMRI) study of mothers with unresolved trauma points to the presence of neurobiological differences, including potential OT dysfunctions, in traumatized mothers that manifest specifically in times of infant distress. When viewing images of their own infant in distress, mothers who have unresolved trauma displayed strikingly blunted responses in the AMY (Kim, Fonagy, Allen, and Strathearn 2014), a brain region abundant in OT receptors (Viviani et al. 2011) and is critically implicated in emotional processing of salient cues (Strathearn and Kim 2013). Although more studies are needed, these studies, when taken together, point to the possibility that OT dysfunction might be implicated in disrupted maternal behavior in general, and during times of infant distress in particular.

Maternal trauma and the infant

Behavior

One common theme that emanates from decades of mother–infant research is the observation that infants of traumatized mothers struggle to turn to their mothers for comfort in times of

distress. When mothers display frightening or frightened behavior (Main and Hesse 1990), engage in disrupted affective communication (Lyons-Ruth, Bronfman, and Parsons 1999), or turn away from their distressed infant (Beebe et al. 2010), the inevitable result is that the infant is left alone with unmitigated distress. The very person to whom the infant is hard-wired to turn for relief is frightening, dissociative, or unavailable. In response, the infant often displays anomalous behavior that reflects fear, anxiety, and ambivalence toward the mother. Examples of this anomalous behavior include approaching the mother and immediately withdrawing, pulling back from the mother with a frightened expression, or freezing. These behavioral patterns, which have been termed disorganized attachment and have received intense scrutiny in the mainstream attachment literature, are considered an infant counterpart of the unresolved state of mind in the adult (Main and Hesse 1990; Main and Solomon 1990). This is the juncture at which the intergenerational transmission of trauma is recognized (van IJzendoorn 1995; Madigan, Bakermans-Kranenburg, et al. 2006): when the mother is traumatized and frightened, the infant also appears frightened and alarmed. Just like their mothers, these infants tend to be insecurely attached rather than securely attached (Madigan, Bakermans-Kranenburg, et al. 2006; Iyengar et al. 2014). The infant's attachment disturbance is conceptually and empirically linked to the mother's unresolved trauma, and this link is mediated by disrupted maternal behavior (Madigan, Bakermans-Kranenburg, et al. 2006), including her frightening or frightened behavior (Hesse and Main, 2006; Schuengel, Bakermans-Kranenburg, and Van 1999), disrupted affective communication (Grienenberger, Kelly, and Slade 2005; Madigan, Moran, and Pederson 2006), or impaired mentalizing (Slade et al. 2005).

Oxytocin

OT is understood to mediate the process by which disrupted maternal behavior alters the normative development of the child. Rodent studies led by Meaney (2001) and Champagne (2008) have provided a fine-grained examination of how early environment molds the neurobiology of the developing child, in turn shaping the child's long-term neurobiobehavioral outcomes. This is what the evolving field of *behavioral epigenetics* investigates: variation in behavioral phenotype as a result of gene–environment interplay, with early social environment (i.e., quality of attachment) seen as one critical component of the interplay (Champagne and Rissman 2011). Compromised maternal behavior in rats, most often displayed by mothers whose brains show low density of OT receptors and low OT production (Francis, Champagne, and Meaney 2000; Champagne et al. 2001), might disrupt the development of the OT system in the offspring. The reduced OT receptor density seen in the offspring's brains is directly associated with compromised level of caregiving in the mother (Champagne et al. 2001; Champagne, Weaver, et al. 2003; Champagne et al. 2006). Like their mothers, these offspring display low OT activity profiles and compromised caregiving behavior subsequently with their own offspring (Francis et al. 1999; Lovic, Gonzalez, and Fleming 2001; Champagne, Francis, Mar, and Meaney 2003). Importantly, cross-fostering studies have shown that these intergenerational effects are primarily a consequence of compromised maternal care received during the offspring's early life (Champagne et al. 2006). These effects could be contingent on the epigenetic regulation of gene expression involving alterations in DNA methylation (Kundakovic and Champagne 2015).

Despite the advances made in this regard in rodent models, the study of corresponding mechanisms in humans is still in its nascent stage due to inherent methodological difficulties of disentangling the reciprocal relations among genetics, epigenetics, and environment. Available studies link compromised maternal behavior to the child's reduced baseline salivary OT levels followed by blunted OT release during social interactions (Feldman, Gordon, and Zagoory-Sharon 2010; Feldman et al. 2013). These intergenerational effects are moderated by OT-related polymorphisms (in the OT receptor gene or the OT gene), such that the presence of high-risk alleles or so-called plasticity genes modulates the child's susceptibility to disrupted maternal care (Belsky and Pluess 2009; Brune 2012; Feldman et al. 2016). An increasing number of studies now link the child's early OT dysfunctions to problems in attachment formation, mentalizing, and social engagement (Clark et al. 2013; Feldman et al. 2013; Feldman et al. 2014). However, longitudinal studies examining OT dysfunctions in infancy as an early biomarker for long-term socioemotional outcomes, including traumatic parenting, are needed for a fuller analysis of the OT system as a neurobiological component of intergenerational transmission.

Now what? Breaking the cycle of intergenerational transmission

Behavior: Insights from earned security and reorganizing research

Although the cycle of intergenerational transmission assumes a rather pessimistic outlook on the socioemotional world of the infant with a traumatized mother, the story does not have to end on a deterministic note. Empirical data support the assertion that change is possible for the mother, which, in turn, can bring about positive developmental outcomes for the infant. This is well reflected in the literature on *earned security*, the term that characterizes the mother who has experienced early trauma but has earned attachment security later in life (Hesse 2008). Earned-secure mothers are classified as securely attached in adulthood. They describe less than optimal early experiences in the AAI but do so in a coherent and reflective manner. This stands in marked contrast to traumatized mothers, who, finding it difficult to assimilate trauma-related information into their autobiographical narrative, display an unresolved state of mind with regard to trauma. Studies have documented that earned-secure mothers are more likely to have received increased support from a significant alternative figure(s) or have engaged in psychotherapy longer (Egeland, Jacobvitz, and Sroufe 1988; Saunders, Jacobvitz, Zaccagnino, Beverung, and Hazen 2011). Despite their early history, earned-secure mothers are as capable as mothers without a history of trauma of providing affectionate, sensitive, and synchronous behavior toward their infants. Not surprisingly, they are often found to have infants who are securely attached (Pearson et al. 1994; Phelps, Belsky, and Crnic 1998; Saunders et al. 2011).

A relevant, yet newly emerging construct is that of *reorganization* (Crittenden and Landini 2011), which captures the dynamic process by which individuals with insecure attachment, unresolved trauma, or both actively "reorganize" their understanding of the past in the direction of resolution of trauma and attachment security. The reorganizing status indicates that an individual has not yet fully resolved his or her trauma, but is actively making changes toward resolution. In the AAI, reorganizing speakers display some slips and incoherence in discourse, which suggest their continued lack of resolution;

however, their discourse also includes reflective statements indicating that they are in the process of flexibly evaluating and assimilating new information to draw meaning from their experience. The construct of reorganization is just starting to receive empirical scrutiny. A small preliminary study involving reorganizing and non-reorganizing mothers with unresolved trauma (Iyengar et al. 2014) recently underscored the potential promise of reorganization in breaking the intergenerational cycle of trauma. Whereas all non-reorganizing mothers with unresolved trauma in the study had infants who were insecurely attached, all reorganizing mothers, despite their unresolved trauma status, were found to have infants with secure attachment. Maternal reorganization emerged as a significant predictor of infant attachment above and beyond maternal unresolved trauma, demonstrating its utility in disrupting the intergenerational transmission of trauma.

OT: Insights from intranasal OT research

The body of OT research reviewed in previous sections lends support to the proposal that early trauma or stress might have the effect of downregulating the functions of the endogenous OT system. The data further suggest that long-term effects of trauma and its intergenerational transmission can be at least partly explained by dysfunctions in the endogenous OT system and the intergenerational transmission thereof. The logic then follows that the pharmacological alterations of the mother's OT might have the potential to protect the mother and the infant from the distressing intergenerational cycle of trauma. This line of thinking has contributed to a rapidly increasing number of studies using intranasally administered OT to determine whether enhancing levels of OT would increase socioemotional functions while ameliorating a range of dysfunctions (Macdonald and Macdonald 2010; Bartz, Zaki, et al. 2011; Bakermans-Kranenburg and van IJzendoorn 2013). Despite the optimism that initially surrounded the promise of OT, results reported to date have been mixed, suggesting a more complicated relationship between OT and trauma. Inconsistencies in reported findings can be partly attributed to the heterogeneity of samples that have been studied and a lack of careful examination of moderating factors, including sex, age, and medication, and among women, reproductive status, menstrual cycle phase, and contraceptive intake. All of these factors have the potential to affect endogenous levels of OT. However, a careful review of the patterns of results that have emerged to date reveals important insights about the nature of the link between early experience and OT.

Three patterns of results have been documented in response to exogenous OT administration. First, consistent with the enthusiasm surrounding the pharmacological potential of OT, several studies have demonstrated that exogenous administration of OT indeed attenuates long-term effects of trauma. OT has been shown to decrease avoidance of perceived social threat (Brune et al. 2013), attenuate stress reactivity (Simeon et al. 2011; Flanagan et al. 2015), increase the experience of attachment security (Buchheim et al. 2009), and reverse trauma-related abnormalities in resting-state brain functioning (Eidelman-Rothman et al. 2015). This is consistent with preclinical data on OT's prosocial and anxiolytic properties. This also substantiates a number of reports, most often obtained from normative, healthy individuals, that have documented effects of exogenous OT on enhancing sensitivity, trust, and mentalizing, while dampening fear and stress responses (Kosfeld et al. 2005; Theodoridou et al. 2009).

These findings have fueled the enthusiasm that OT might be capable of reversing the abnormalities observed in traumatized mothers and their infants.

However, the initial enthusiasm has been gradually tempered by studies documenting that exogenously administered OT fails to yield significant effects in some individuals with early trauma or stress. Most often, when control subjects are examined alongside those with a history of trauma, a pattern emerges wherein OT is found to exert its prosocial effects in controls, whereas the beneficial effects are diminished or absent in those with trauma (Meinlschmidt and Heim 2007; Feeser et al. 2014). We understand these seemingly divergent effects, moderated by the presence of trauma, as potentially reflecting the early alteration of the OT system at the level of the receptor (Kim, Soeken, et al. 2014). Rodent studies of early epigenetic programming of the OT system have documented that suboptimal early social environment leads to fundamental changes at the OT receptor level (Branchi et al. 2013; Champagne et al. 2001; Champagne, Weaver, et al. 2003; Champagne et al. 2006). Although corresponding data are lacking in humans, the lack of response to exogenous OT seen in individuals with early trauma or stress might be a reflection of alterations in OT receptor density, function, or affinity that occurred during the developmental process (Bakermans-Kranenburg and van IJzendoorn 2013).

Perhaps the results that have been most puzzling are those demonstrating exacerbations of existing trauma-related dysfunctions as a result of exogenous OT administration. Referred to as paradoxical effects of OT in the literature, this pattern of results has been repeatedly found in individuals with insecure attachment history, early adversity, or trauma, and rarely seen in those with secure early history. Some reports show that OT administration leads to increased negative social emotions (Shamay-Tsoory et al. 2009), decreased memories of care and closeness (Bartz et al. 2010), and reduced trust (Bartz, Simeon, et al. 2011; Ebert et al. 2013) in individuals with early trauma or stress. In attempts to reconcile the observed paradoxical effects with the prevailing view of OT as a prosocial neuropeptide, alternative hypotheses have been proposed: rather than universally enhancing socioemotional functions, some have suggested that OT might have the effect of increasing the salience of social cues (Shamay-Tsoory 2010), activating affiliative motives (particularly in interaction with mesolimbic DA motivational circuitry; Tops 2010; Walker and McGlone 2013), or mobilizing approach behaviors (Kemp and Guastella 2010; Feeser et al. 2014). Note that all three changes could lead to increased prosocial behavior in individuals with secure attachment histories, but conversely might intensify negative emotions and exacerbate existing dysfunctions in individuals who have experienced early adversity. When increased OT highlights the salience of social cues, activates affiliative motives, or increases approach behaviors, traumatized individuals might be reminded of past experiences in which affiliation has been unsuccessful, leading to concerns about trust and closeness (Bartz, Simeon, et al. 2011). The link between downregulated OT systems and early trauma and stress could then even be seen as a protective mechanism aimed at maintaining emotional equilibrium in individuals with trauma and stress. Blunted OT, although compromising a range of adaptive socioemotional functions, might also serve to blunt the distressing effects of unresolved trauma. To abruptly increase levels of OT in these individuals via exogenous administration might override the mechanism that maintains their stability and bring out, or even amplify, their underlying vulnerability to unresolved emotional distress.

Synthesis

Given the null and paradoxical effects, which are more prevalent in individuals with a history of early trauma or stress, it appears that artificially increasing the level of OT alone does not itself offer promise of breaking the cycle of intergenerational transmission of trauma. Although the field has not yet reached a consensus on whether OT should primarily be viewed as increasing the salience of social stimuli, activating affiliative motives, or mobilizing approach-related behaviors, we understand that the outcome of any one of these would vary as a function of the individual's underlying expectations about the self, others, and relationships.[4] Individuals with unresolved trauma, who have had repeated experiences wherein their safety and security were undermined in relationships, are likely to operate from the belief that their desire to relate is most often met by undesired outcomes, even when this belief is outside of their conscious awareness. Without addressing the underlying belief about disrupted relationships, increasing the salience of social behaviors or the drive to approach and relate will most often be unhelpful and likely counterproductive. Processing and resolution of trauma, which allows for re-evaluation and restructuring of long-held expectations about relationships, is therefore the paramount task facing these mothers. To use the terms from the attachment literature, mothers should foremost be engaged in the process of reorganization so that they can become earned secure. As this process unfolds, the use of exogenous OT could prove to be helpful in amplifying the salience of new relational experiences that gradually bring about adaptive changes in one's long-held beliefs. OT could also be used to augment affiliative motives at a point where such intervention might be beneficial rather than threatening.

Theoretical and clinical gaps still exist with regard to the use of exogenous OT as a therapeutic agent or adjunct. More data are needed to clarify the nature of OT dysregulation depending on the type, timing, duration, and recurrence of trauma. Larger and more rigorously controlled studies are needed to account for the role of moderators known to affect endogenous levels of OT. The effect of repeated administration of exogenous OT on long-term endogenous OT release should also be studied more carefully, along with the nature of OT's interaction with other pharmacological agents that can be used to treat trauma-related conditions.

Conclusion

This paper examined Fraiberg's "ghosts in the nursery" in four ways: first, by examining the intergenerational transmission of trauma as observed in behavior and parenting; second, by reviewing the intergenerational transmission of OT dysfunctions, as mediated by traumatic parenting; third, by evaluating the latter as a neurobiological substrate of the former; and fourth, by synthesizing behavioral and OT research to consider how intergenerational transmission can be reversed.

The importance of processing and working through trauma cannot be underscored more, both in Fraiberg's times and in the present. However, recent advances in neuroscience have allowed a detailed delineation of a potential neurobiological mechanism that could account for the phenomenon of intergenerational transmission that has long been observed. With the neurobiological framework presented in this paper, we are in the

position to identify, with a greater specificity, mechanisms that might be suitable targets of prevention and intervention efforts, both on behavioral and neurobiological levels.

Notes

1. This is at times referred to as the *unresolved state of mind* throughout this paper. Readers should be advised that some differences exist in the conceptualization of unresolved trauma, along with other attachment classifications, between different schools of attachment theory (mainstream attachment theory led by Main vs. dynamic maturational model led by Crittenden). However, detailing the differences is beyond the scope of this paper, which synthesizes relevant research from both schools. Interested readers should refer to Cassidy and Shaver (2008) and Crittenden and Landini (2011) for an overview of these two schools of thought.
2. Corticosterone is the dominant glucocorticoid in rodents, whereas cortisol is more dominant in humans.
3. The pattern of associations described in this section and the following two sections are represented visually in Figure 1.
4. Often referred to as mental representations or internal working models (Bowlby 1973).

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