Hormonal and non-hormonal bases of maternal behavior: The role of experience and epigenetic mechanisms

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Abstract

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Though hormonal changes occurring throughout pregnancy and at the time of parturition have been demonstrated to prime the maternal brain and trigger the onset of mother–infant interactions, extended experience with neonates can induce similar behavioral interactions. Sensitization, a phenomenon in which rodents engage in parental responses to young following constant cohabitation with donor pups, was elegantly demonstrated by Rosenblatt (1967) to occur in females and males, independent of hormonal status. Study of the non-hormonal basis of maternal behavior has contributed significantly to our understanding of hormonal influences on the maternal brain and the cellular and molecular mechanisms that mediate maternal behavior. Here, we highlight our current understanding regarding both hormone-induced and experience-induced maternal responsibility and the mechanisms that may serve as a common pathway through which increases in maternal behavior are achieved. In particular, we describe the epigenetic changes that contribute to chromatin remodeling and how these molecular mechanisms may influence the neural substrates of the maternal brain. We also consider how individual differences in these systems emerge during development in response to maternal care. This research has broad implications for our understanding of the parental brain and the role of experience in the induction of neurobiological and behavior changes.

Introduction

Hormonal changes occurring during gestation serve a critical role in altering maternal physiological and neuroendocrine systems to facilitate fetal development and prepare the mother for parturition and lactation. These hormones also induce both short- and long-term changes in the maternal brain that contribute to maternal behavior during the postnatal period. Estrogen and progesterone priming with downstream consequences for prolactin and oxytocin systems have been explored extensively in the context of maternal behavior, with converging evidence from both pharmacological and genetic studies illustrating the mediating role of these hormones. However, maternal behavior can occur in the absence of hormonal priming. In a seminal paper titled “Nonhormonal Basis of Maternal Behavior in the Rat” published in Science in 1967, Jay Rosenblatt established empirical evidence for the role of exposure to pups in eliciting maternal behavior among both male and female adult rats (Rosenblatt, 1967). These findings were striking and suggestive that although hormones may influence the onset of maternal responses during the postnatal development of offspring, experience with offspring could similarly trigger these behavioral responses. These initial findings have formed the basis of many ongoing research avenues within the study of the maternal brain. In particular, recent studies of experiential effects on maternal behavior have highlighted the critical role of epigenetic mechanisms in shaping maternal responses. Here, we will describe how the ongoing study of the non-hormonal basis of maternal behavior has contributed to these research themes and the implications of this research for our understanding of variation in the parental brain.

Non-hormonal basis of maternal behavior

Rosenblatt (1967), expanding on the work of Weisner and Sheard (1933), demonstrated that hormonal stimulation is not required to induce the onset of maternal behavior in rats. Using an experimental design in which rats were housed continuously across consecutive days with 5–10 day old pups, maternal responses (retrieving and licking of pups, crouching over pups, nest-building) were found to emerge in both male and female adult rats within the period of 10–15 days (Rosenblatt, 1967; Weisner and Sheard, 1933). The process by which continual exposure to pups induces maternal responses in rats has been termed sensitization. The discovery of the phenomenon of sensitization was groundbreaking and addressed several fundamental questions regarding the nature of maternal behavior. First, continual cohabitation with pups induced the onset of maternal behavior in
nearly all the rats tested. This finding suggests that the neural substrate that supports caregiving behaviors must exist in rats of both sexes and activation of these systems can occur in the absence of hormone stimulation. Subsequent studies building on this finding have demonstrated that the hormonal events of pregnancy and birth function to reduce the amount of exposure to pups that is sufficient to induce caregiving behaviors (Siegel and Rosenblatt, 1975a,b). Second, the findings reported in Rosenblatt (1967) suggest that circulating ovarian and/or pituitary hormones are not involved in the pup-induced onset of maternal behavior. Removal of the ovaries or pituitary gland did not delay the onset of maternal behavior. Third, cohabitation with pups was not found to alter estrous cycling in gonad intact virgin females, suggesting that sensitization is not mediated by pup-induced changes in peripheral steroid hormone secretion. More recently, it has also been determined that pup-induced maternal behavior is not mediated by local steroid hormone production within the brain (neurosteroids). Transgenic mice lacking a functional copy of the aromatase gene, which is required for synthesis of estradiol in the brain and periphery, show sensitization that is not significantly different from virgin female mice (Stolzenberg and Rissman, 2011).

Though the induction of maternal behavior through repeated pup exposure is not likely to occur under natural conditions (pups would not survive without milk), study of the non-hormonal basis of maternal behavior in rats has facilitated the investigation of the neural substrate upon which hormonal fluctuations during pregnancy and birth act to induce maternal behavior (Mayer and Rosenblatt, 1979). Rosenblatt described the non-hormonal and hormonal bases of maternal behavior as distinct processes that are mediated, at least in part, by overlapping or common mechanisms (Rosenblatt et al., 1988). For example, the onset of maternal behavior (hormonal or non-hormonal) involves the modification of two classes of behavioral responses toward pups. For the neophagic female rat, fear responses must be inhibited toward novel pups. However, reducing fearful aggression is not sufficient for a rapid onset of maternal behavior (Fleming, 1989; Fleming and Rosenblatt, 1974a,b). A rapid onset of maternal behavior (hormonal or non-hormonal) also requires an increase in approach responses toward pups, suggesting the role of neural systems involved in motivation. Understanding of the distinct vs. common pathways underlying hormonal and non-hormonal maternal responses in rats may also facilitate the investigation of the neural systems that sustain maternal care over the course of the extended postpartum period (Numan, 2006, 2015; Numan and Insel, 2003; Numan and Stolzenberg, 2009). Pregnancy hormones are involved in priming the brain to respond to infant stimuli. However, hormone levels reduce significantly within a few hours of birth, and the long-term maintenance of maternal behavior throughout the postpartum period is hormone-independent (Bridges, 1975; Numan, 2015; Numan and Insel, 2003; Rosenblatt, 1975a).

**Hormonal basis of maternal behavior**

Our understanding of the molecular and neural pathways through which pup exposure comes to alter maternal behavior requires consideration of the pathways through which hormones influence maternal behavior. The pattern of pregnancy hormone stimulation that primes the rodent maternal brain begins at mating when cervical stimulation initiates a twice-daily pattern of prolactin release from the anterior pituitary (for approximately 9–10 days after mating) that functions to prevent degradation of the corpora lutea (Terkel and Sawyer, 1978). Consequently, there is a steady increase in progestrone (P) during the first part of pregnancy, which prepares the uterine endometrium for implantation and maintains a uterine environment that promotes growth of the embryo (Csapo and Resch, 1979a,b; Zakar and Hertelendy, 2007). At mid-pregnancy, placental lactogens support the luteal secretion of P that is necessary for the continuation of pregnancy. Whereas rising levels of P promote the maintenance of pregnancy, the decline of P beginning in mid-pregnancy initiates a shift in hormonal events that eventually regulate the timing of parturition. Increasing levels of estradiol (E) secreted from the ovary prepare the uterine endometrium for labor by promoting rhythmic contractility of the uterus, and the sharp decline in P just before birth removes the inhibitory tone on the uterine muscles and allows them to respond to the surge in oxytocin (OT) from the posterior pituitary that induces uterine contraction and labor (Hertelendy and Zakar, 2004; Zhang et al., 1992).

Though the pregnant rat is exposed to circulating levels of pregnancy hormones, responsiveness toward pup stimuli is delayed until the final hours prior to parturition (Mayer and Rosenblatt, 1984). Rosenblatt hypothesized that the hormonal fluctuations present at this time may also prime the brain to respond to infant stimuli. Testing this hypothesis, it was determined that factors circulating in the blood at the time of birth and just after birth were responsible for initiating maternal responsiveness (Terkel and Rosenblatt, 1968, 1972) and could induce shortened (but not immediate) sensitization latencies in the virgin rat. Artificial termination of pregnancy by hysterectomy (removal of uterus and fetuses) during the latter half of pregnancy, which results in a decline in P and rise in E secretion produces an immediate onset of maternal behavior when pups are presented 48 h after surgery (Rosenblatt and Siegel, 1975). It is evident that the combined decline in P and elevation in E are necessary for the rapid induction of maternal behavior (Siegel and Rosenblatt, 1978). Thus, hormonal changes throughout pregnancy play a role in gradually shifting the behavioral responses of females and to trigger responding to pups at parturition. These hormonal changes influence several neural systems, and in particular modify hormone receptor levels and neural activity within the medial preoptic area of the hypothalamus (MPOA) (Numan, 2015; Numan and Insel, 2003). Estradiol benzoate (EB) implants in the MPOA of 16-day-pregnant hysterectomized--ovariectomized females induces a rapid onset of maternal behavior (Numan et al., 1977). Moreover, pregnancy hormones have been found to increase estrogen receptor distribution and binding in the MPOA (Giordano et al., 1989, 1991), which contributes to the cellular and molecular changes that shape the maternal brain.

**Interplay between hormones and epigenetics in organizing maternal responsivity**

Estrogen acts through multiple cellular/molecular pathways to alter neural function and behavior (Numan, 2015; Stolzenberg and Numan, 2011; Vasudevan and Pfaff, 2008). However, the best characterized route of action involves estradiol-induced changes in gene transcription. Estradiol alters the transcription of estrogen responsive genes by binding estrogen receptors (ERα and ERβ), which are ligand-activated transcription factors. The ERα and ERβ receptor subtypes share almost 100% amino acid homology, but are encoded by different genes and have distinct transcriptional consequences (Delaunay et al., 2000; Katzenellenbogen and Katzenellenbogen, 2000). At these sites, ERs assemble multi-protein complexes, which function to remodel chromatin, recruit transcriptional machinery, and induce gene transcription (Green and Carroll, 2007; Mann et al., 2011; Nilsson et al., 2001). Estrogen receptors also recruit repressive protein complexes involved in silencing gene expression.

Within the nucleus, transcription factor action at DNA sequences is ultimately regulated by chromatin structure. Chromatin refers to DNA and the histone protein octamers that the DNA is wound around. The packaging of chromatin within the nucleus has dramatic effects on gene regulation. Tight chromatin configurations block access of transcriptional machinery to transcription start sites, resulting in gene silencing (Razin, 1998). Following ligand binding, the transcriptional domain of ER interacts with proteins in the p160 coactivator family to recruit additional proteins, which modify the structure of chromatin in order to induce gene transcription (Nilsson et al., 2001). In this context, chromatin remodeling is mediated by post-translational modifications
of histone protein tails, which alter the strength of association between histones and DNA and/or altering transcription factor binding. For example, histone acetylation neutralizes the positive charge of histone proteins, “loosening” their association with negatively charged DNA, and increasing transcription factor access to DNA sequences (Peterson and Laniel, 2004). Histone acetyltransferase (HAT) enzymes catalyze the transfer of acetyl groups to histone protein tails, whereas histone deacetylase (HDAC) enzymes remove them. The addition of acetyl groups to histone protein tails at specific lysine residues (H3K14, H4K5, H4K8) is associated with increased transcription of estrogen responsive genes. For example, the p160 coactivator protein SRC1 recruits CREB binding protein (CBP), p300, and CBP/p300 associated factor (PCAF), which engage in HAT activity (Sheppard et al., 2003). p160 coactivators also recruit histone methyltransferase enzymes such as CARM1, MLL1, and MLL3, which methylate histone protein tails and facilitate the transcription of ER-induced genes (Ansari et al., 2011; Teysseir et al., 2002). Histone methylation can have activating or repressive effects on gene expression through the recruitment of additional proteins that regulate transcription (Wozniak and Strahl, 2014). Finally, although the majority of research on ER signaling and chromatin remodeling has focused on breast cancer and MCF7 cells, a recent study suggests that the mechanisms described above may also play a role in the ER-mediated onset of female sexual behavior in mice. Cagnidze et al. (2013) provide direct support for the idea that ER regulation of gene expression is associated with E-induced histone acetylation in the promoter region of the oxytocin receptor and progesterone receptor genes in the ventromedial nucleus of the hypothalamus. Estradiol also increased the expression of SRC1, p300, and MLL3 genes (Cagnidze et al., 2013). The extent to which these modifications play a critical role in the hormonal onset of maternal behavior is an important question for future research.

**Interplay between experience and epigenetics in organizing maternal responsivity**

Sensitized female rats are not exposed to pregnancy hormone priming, and yet the experience of interacting with pups results in activation of neurons within the MPOA of a sensitized virgin female comparable to that observed in a lactating dam (Komisaruk et al., 2000; Numain, 2015). If pup experience does not affect circulating levels of E, how can pup exposure lead to a similar activation of MPOA neurons? Within the MPOA, intracellular signals that have been linked to the onset of mothering include altered calcium signaling and phosphorylation of extracellular regulated kinase (ERK) and cyclic AMP response element binding protein (CREB) (Jin et al., 2005; Kuroda et al., 2007). Functionally, mice lacking CREB or FoB (downstream from FosB) experience disruptions in the onset of maternal behavior (both hormonal and non-hormonal), whereas other hypothalamic-mediated behaviors remain intact (Brown et al., 1996). Comparison of the MPOA of sensitized vs. lactating rats and mice indicate that unlike estradiol action at ERs, which is exclusively associated with parturition, these pathways are activated to a similar extent in sensitized virgins and lactating dams when interacting with infants.

A summary of the proposed signaling mechanisms in the MPOA that may mediate maternal behavior is illustrated in Fig. 1. Much like ER, these signaling pathways can dynamically impact gene expression and recruit chromatin-modifying enzymes to transcription start sites (Cortes-Mendoza et al., 2013; Riccio, 2010). Thus, the downstream molecular events of experience and hormone stimulation may be similar for maternal female rodents, particularly the alterations in chromatin. In support of this hypothesis, a striking degree of overlap has been reported in the genes upregulated by the hormonal and experiential induction of maternal behavior in mice (Stolzenberg et al., 2012). For example, genes encoding the CBP, ERs, oxytocin, vasopressin, and vasopressin receptor proteins are upregulated in both sensitized virgin and lactating mice. Among sensitized virgin mice, experience with pups alone was capable of affecting the expression of at least one estrogen receptor subtype: ERβ (Stolzenberg et al., 2012). Further, increased expression of CBP may contribute to experience-induced chromatin remodeling as CBP is recruited to both the ERβ and oxytocin gene promoters in sensitized females (Stolzenberg et al., 2014). Moreover, systemic administration of the HDAC inhibitor sodium butyrate reduced the amount of pup experience required to induce maternal behavior in virgin mice. Importantly, HDAC inhibitor treatment also induced molecular changes within the MPOA that have been observed following sensitization (Stolzenberg et al., 2014). Repeated experiences with pups may facilitate long-term maternal responsivity by activating intracellular signaling pathways that recruit chromatin-modifying enzymes and initiate gene transcription in MPOA neurons. This idea is supported by the finding that relatively brief experiences with pups, which typically fail to impact maternal behavior long-term, can be potentiated to do so with HDAC inhibitor treatment. Thus chromatin remodeling facilitates both hormone and non-hormone dependent maternal behavior, suggesting that this is a shared mechanistic pathway accounting for maternal responsivity in lactating and non-lactating females (see Fig. 2).

**Developmental origins of hormonal and non-hormonally induced maternal behavior**

Though the hormonal exposures associated with pregnancy and parturition clearly facilitate maternal behavior, it is also evident that there is variation in maternal responding that can be observed in both lactating and non-lactating females. Interestingly, this variation is induced through the experience of maternal behavior itself. Virgin female rats that have experienced elevated levels of maternal care during their own postnatal development exhibit reduced latency in days to display maternal behavior within the daily pup-exposure paradigm (Champagne et al., 2001). This reduced latency can also be observed in pre-pubertal female offspring that experienced high levels of
maternal licking-grooming (LG) during the first postnatal week (Pena et al., 2013). Following mating and parturition, these females also exhibit increased maternal behavior (particularly LG and arched-back nursing) toward their offspring (Champagne et al., 2003a). This behavioral variation in both lactating and non-lactating females does not appear to be the consequence of differences in circulating hormones. Adult ovariectomized virgin females that have experienced low vs. high levels of LG during infancy differ in their responsiveness to EB. Among ovariectomized females that had experienced high levels of LG, EB induces increased c-fos activation within the MPOA and increased oxytocin receptor binding within the MPOA and lateral septum (Champagne et al., 2001, 2003b). In contrast, EB-induced changes in the MPOA and lateral septum were not observed in ovariectomized females that had experienced low levels of LG. Reduced levels of hypothalamic ER\(\alpha\) likely mediate this differential sensitivity to estradiol and developmental studies indicate that increased LG experienced during infancy results in elevated ER\(\alpha\) levels within the MPOA that is apparent at postnatal day 6 and is maintained through to adulthood (Champagne et al., 2001, 2003b; Pena et al., 2013).

Exploration of the cellular and molecular mechanisms through which variation in maternal behavior shapes maternal responsivity and postpartum maternal care provides further demonstration of the critical role of chromatin remodeling in the maternal brain (see Fig. 3). During postnatal development, high levels of LG induce increased Stat5b transcription factor levels within the MPOA and increased Stat5b binding to the promoter region of the \textit{Esr1} gene (encoding ER\(\alpha\)) (Champagne et al., 2006). Stat5b activation within the promoter likely contributes to the reduced levels of H3K9 tri-methylation (a repressive chromatin mark) and increased H3K4 tri-methylation (a marker of transcriptional activation) at the \textit{Esr1} gene promoter observed in offspring reared by dams that engage in high levels of LG (Pena et al., 2013). These epigenetic changes contribute to the transcriptional activation of \textit{Esr1} in response to LG and accounts for increased ER\(\alpha\) mRNA levels observed in the MPOA during the postnatal period. The maintenance of elevated ER\(\alpha\) mRNA levels into adulthood is associated with decreased 5-methyl-cytosine methylation within the \textit{Esr1} gene promoter, whereas offspring that experience low maternal LG are observed to have increased levels of \textit{Esr1} DNA methylation (Pena et al., 2013). Though the signaling pathways through which Stat5b levels and chromatin remodeling are induced by LG have yet to

![Fig. 2. A hypothetical model for the involvement of epigenetic mechanisms in the regulation of MPOA neuronal activity in maternal responding. In a non-maternal female rodent, neurons in the MPOA receive pup-related inputs, but these inputs culminate in little, if any, CBP recruitment, histone acetylation and gene expression. In the MPOA of maternal females, interaction with pups increases CBP recruitment, acetylation, and gene expression. Abbreviations: Ac — acetyl group; CBP — CREB binding protein.](image-url)

![Fig. 3. Proposed model through which the experience of postnatal maternal care induces lasting epigenetic changes within the MPOA. The experience of high levels of LG is associated with increased Stat5b levels that may bind to the \textit{Esr1} gene promoter and induce histone modifications (acetylation and methylation) that increase \textit{Esr1} transcription. Transcriptional activation reduces the likelihood of epigenetic gene silencing through DNA methylation and leads to long-term up-regulation of ER\(\alpha\) levels. Elevated estrogen levels during pregnancy/lactation activate these receptors resulting in up-regulation of ER sensitive genes (e.g. oxytocin receptor) and promoting increased maternal behavior. Abbreviations: Ac — acetyl group; ER — estrogen receptor; \textit{Esr1} — gene encoding estrogen receptor \(\alpha\); Me — methyl group; \textit{Oxtr} — oxytocin receptor.](image-url)
be elucidated, the interactions between Stat5b and P300/CBP suggest the possibility of recruitment of acetyltransferases/methyltransferases to \(Esr1\) (Pfizter et al., 1998). This mechanistic route further demonstrates parallels to estrogen-mediated effects.

**From mother–pup interactions to epigenetics**

The molecular impact of experience with pups (sensitization in adulthood) or experience of pups (effects of maternal care during development) that has been documented raises critical questions as to how these broad sensory/social experiences come to induce these downstream epigenetic consequences. These questions have yet to be systematically addressed. It is certainly the case that neuronal activation can induce epigenetic variation, and this may be a mechanism underlying neuronal plasticity in response to sensory stimulation (Colquitt et al., 2014; Putignano et al., 2007). CREB and ERK signaling pathways may have particular functional relevance to these sensory-mediated effects (Putignano et al., 2007). Somatosensory inputs from pups likely contribute to the expression of maternal behavior (hormonal or non-hormonal) and deprivation of this contact can impact the maternal brain (Pedersen et al., 1995). Tactile-mediated sensory input may also be critical to the epigenetic impact of the experience of maternal care during postnatal development (Hellstrom et al., 2012). The impact of maternal deprivation can be augmented by provision of high levels of “licking-like” tactile stimulation (in combination with olfactory cues from siblings) (Melo et al., 2006) and this form of sensory input during infancy can alter DNA methylation within the \(Esr1\) promoter region in the MPOA and amygdala (Edelmann and Auger, 2011; Kurian et al., 2010). However, progress in our understanding of how the interactions with pups or that pups have during development come to be transduced into long-term molecular signatures within the brain will require in depth analyses of the temporal dynamics of neural and epigenetic variation in response to these experiences.

**Maternal experience and the mesolimbic dopamine system**

Though studies of the hormonal and non-hormonal bases of maternal behavior have focused primarily on hypothalamic regions such as the MPOA, similar to all complex behavioral phenotypes, there are contributions by a broad range of neural circuits. Particularly relevant to the motivational aspects of pup-directed behavior, the mesolimbic dopamine system plays a critical role in maternal behavior. Striatal depletion of dopamine (DA) (Hansen et al., 1991) and pharmacological antagonism of DA receptors in the nucleus accumbens (NA) (Keer and Sterin, 1999) results in impaired maternal behavior. Interference with neural activity within the ventral tegmental area (VTA) or connectivity between the MPOA and mesolimbic dopamine system abolishes maternal behavior in lactating female rats (Numan et al., 2005, 2009; Numan and Smith, 1984). Lactating females that engage in interactions with pups have elevated dopamine release in the ventral striatum and NA (Champagne et al., 2004; Hansen et al., 1993) and females that engage in higher levels of maternal care have increased dopaminergic projections from the VTA to the NA (Shahrkoh et al., 2010). Both pup sensitization and parity result in enhanced dopamine release in response to pup cues and hormonal treatments that enhance pup sensitization also enhance DA release in the NA (Afonso et al., 2008, 2009, 2013) and stimulate signaling through D1 receptors (Stolzenberg et al., 2010). These experience-dependent changes may account for the maintenance of maternal behavior following the reduced hormone levels occurring in the postpartum period and account to the long-term enhancements in maternal behavior as a function of previous interactions with pups (Lee et al., 1999, 2000). The role of epigenetic changes in these short- and long-term effects of maternal experience within the mesolimbic dopamine system has yet to be explored.

The experience of variation in maternal care during infancy has significant effects on developing mesolimbic dopamine pathways, thought similar to the case of hormonally or non-hormonally induced maternal behavior, the role of epigenetic mechanisms within these pathways has not been determined. Low levels of LG during postnatal development results in reduced dopaminergic projections from the VTA and reduced D1, D2, and D3 receptor mRNA levels in the NA of female offspring (Pena et al., 2014). Reduced DA release in response to pup stimuli is observed in females deprived of maternal care and this rearing effect can be attenuated if pups receive tactile stimulation (Afonso et al., 2011). Though transient and long-term changes in gene expression are observed within mesolimbic pathways in response to maternal care, specific targets of epigenetic variation within these pathways have not been identified. Interestingly, epigenetic variation in the MPOA may account for variation in the VTA as transcriptional up-regulation of \(Esr1\) in the MPOA leads to increased DA projections from the VTA and reduced latency to maternal behavior in non-hormonally primed females (Pena and Champagne, in press). Connectivity between the MPOA and the mesolimbic DA system likely plays a critical role in coordinating hormones, experience and motivation to engage in maternal care.

**Conclusions & implications**

Maternal responsiveness to offspring is critical to offspring survival and development. In mammals, the hormonal changes occurring during pregnancy and at the time of parturition have been demonstrated to alter maternal behavioral and physiological functioning to promote nurturing responses. However, despite the pivotal role of hormones, experience with offspring can likewise induce maternal behavior. The study of the non-hormonal basis of maternal behavior has revealed both the unique processes and common downstream mechanisms that are evident in hormone and non-hormonal dependent responses to neonates. In general, the behavioral responses of a sensitized virgin toward pups match that of a lactating dam both in terms of variety and sequence (Rosenblatt, 1975b). Motivation to gain access to pups is heightened in lactating dams compared to sensitized virgins (Bridges et al., 1972; Seip and Morrell, 2008). However, even these behavioral differences can be overcome by increasing the level of experience with pups among virgin females (Seip and Morrell, 2008; Stolzenberg and Rissman, 2011). At a mechanistic level, hormone and non-hormonal dependent responses to neonates can be attributed to epigenetic remodeling within the hypothalamus that promotes transcriptional activation within estrogen receptors and their downstream targets. These pathways are responsive to estrogen, experience with pups, and the developmental experience of maternal care. Collectively, this research highlights the degree of plasticity within the maternal brain in response to broad environmental signals.

Understanding of experience-induced changes in the maternal brain that contribute to mother–infant interactions has implications for both basic and translational research (Numan, 2015). Our current knowledge regarding the timecourse of experience-induced cellular and molecular changes that account for lasting changes in behavior is limited. However, our ability to apply in vivo imaging and manipulation in these systems is becoming increasingly sophisticated and may yield critical insights into the interplay between experience and chromatin remodeling events within genes critical for maternal behavior. From a translational perspective, elucidation of these mechanisms may provide insights into the neurobiological basis of parenting across a diverse range of parenting strategies. There is increasing use of in vitro fertilization and surrogacy, which may alter the hormonal profile of mothers during the postpartum period, however the impact on parental responsiveness has not been explored. There is a cultural shift associated with human parenting, such that fathers have an increasing role in the care of infants/children. Neuroimaging studies suggest that both mothers and fathers display neuronal activation in response to infant cues and that the time spent in direct childcare by the parent is a significant predictor of this activation (Abraham et al., 2014). Consistent with the finding...
reported by Rosenblatt (1967), both males and females can be induced to achieve the same behavioral state through experience with neonates. However, the unique vs. common routes through which this may occur are not known. Finally, the interaction between sex and hormones is likely critical for our understanding of the long-term effects of parenting experience for the parental brain and for parental behavior toward offspring.

References


