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## Reactivity, regulation, and reward responses to infant cues among mothers with and without psychopathology: an fMRI review

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### Abstract

Despite important progress in understanding the complex caregiving system, developmental research has only recently begun to focus on the mother's internal affective state and its role in sensitive caregiving behavior. This review will summarize recent findings of functional neuroimaging research to elaborate on the neural components associated with maternal sensitive care or disrupted responsiveness to infant communications. First, maternal emotion reactivity and regulation, as well as maternal reward responsiveness to infant cues, will be reviewed among healthy mothers. Then, emotion and reward-related processes among mothers who display sensitive versus disrupted caregiving will be explored. Finally, these patterns of response will be compared to patterns of response among mothers with psychiatric disorders, including depression, posttraumatic stress disorder, and substance abuse. The aim of this review is to examine whether differences in emotion reactivity and regulation, as well as in the encoding of infant stimuli as rewarding, are related either to maternal psychopathology or to maternal difficulties in responding promptly and appropriately to their infants. A summary of the challenges facing developmental neuroscience research in furthering our understanding of maternal responses to infants will close this review.

### Keywords

maternal emotion regulation; fMRI; review; PTSD; substance abuse; depression; attachment; infancy

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According to developmental theory, the function of the caregiving system is to protect the infant and increase the infant's chances for reproductive fitness (1, 2). Studying mothers' affective reactivity, regulation, and reward processes associated with infant cues is critical because the maternal caregiving system during infancy sets the stage for the child's

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development of a secure attachment and adaptive socio-emotional competencies (2). Maternal sensitivity, defined as ‘the ability to respond appropriately and promptly’ to the infant’s signals, is one component of the caregiving system that has been demonstrated to be an important foundation for the infant’s development of a secure attachment and for adequate stress regulation (3). Thus, once activated by cues signaling distress for the child, the caregiving system employs a repertoire of behaviors designed to comfort and sooth the infant, such as responding to infant signals, smiling, and increasing proximity. Once the infant is comforted, the caregiving system is thought to be deactivated and mothers will experience rewarding feelings of pleasure and satisfaction. Affective and reward mechanisms may therefore play a critical role in the motivation to engage in sensitive caregiving (2).

Sensitive caregiving has been associated with lower child negativity and better effortful control as a marker of child regulatory behavior [for a review, see (4)]. Often described as ‘intuitive parenting’, it has been observed that caregivers may rapidly read the infant’s signals and intuitively adapt their preverbal communication to attend to the child’s need [for a review, see (5)]. For example, in a still-face procedure, infants of more sensitive mothers or of mothers exhibiting more positive affect or involvement showed more regulatory behaviors (e.g. self-soothing), more positive affect, and less negative affect (6). Impairments in sensitivity, indexed by higher levels of disrupted caregiving behaviors (e.g. withdrawal or intrusiveness) have also been reported among mothers with depression (7, 8), posttraumatic stress disorder (PTSD) (9, 10) and substance abuse (11). Disrupted maternal behaviors predict infant disorganized attachment behavior (12) and can have negative consequences for the child’s further cognitive and socio-emotional development (13–17). Despite progress in understanding the complex caregiving system, behavioral and questionnaire studies to date offer little insight into mothers’ *internal* processes to infant cues and their role in sensitive versus disrupted communication with the infant. Instead, the child’s emotion regulation processes, and the parental socialization practices corresponding to child regulation have been the primary focus of developmental literature (4, 18). To improve our understanding of mechanisms of caregiving behavior, recent studies have begun to investigate mothers’ emotion reactivity and regulation to infant communications, as well as their encoding of infant cues as rewarding.

Although research on maternal parenting behavior has roots in animal studies (e.g. 19), it is also important to evaluate human mother’s affective responses as mother-infant interactions are complex (20). The current paper reviews functional magnetic resonance imaging studies examining maternal responses to infants’ visual or auditory cues. More specifically, we focus on mothers’ emotion reactivity and regulation in response to infant affective cues and on the reward salience of those cues to better understand complex mother–infant interactions. To achieve this aim, we will first review the role of emotion reactivity, emotion regulation, and reward processes among mothers without psychopathology, in relation to a range of caregiving behavior from sensitive to disrupted communication with their infants. Second, we will summarize findings on affective and reward processing to infant cues among mothers with major depressive disorder (MDD), PTSD and substance abuse as these have been related to differences in caregiving behavior. Finally, consideration of the usefulness of focusing on distinct affect and reward responses to understand differences in

maternal responses to their infants followed by a brief review of factors likely to pose a challenge to interpreting outcomes in future studies will close this review.

## Emotion reactivity, emotion regulation, and reward responses

Based on the principles of temporal dynamics of emotional responding (affective chronometry) (21) and the dual-process model of emotion regulation (22), affective stimuli in the environment can elicit an emotional reaction and a regulatory response. As part of the limbic system, the amygdala plays a critical part in the immediate reactivity to emotionally salient stimuli in the environment to facilitate learning (23, 24). Further an emotional response is associated with an implicit and explicit emotion regulatory response (22). While explicit emotion regulation refers to the alterations of existing emotional responses through top-down processes available to conscious awareness [e.g. cognitive reappraisal (25)], *implicit* or *automatic* emotion regulation is evoked by the stimulus itself and occurs outside of the individual's awareness (26). Neuroimaging studies of implicit emotion regulation have suggested an inverse relationship between the limbic system, including the amygdala, and regions of the prefrontal cortex (PFC) (27, 28). As shown by time-series studies of mother–infant face-to-face interaction, mother and infant are influencing one another in intervals as small as 1/3 of a second (29); for adult communication see also (30). Mothers' affective responses will ensure their recognition of infant's signals while an appropriate regulation of the initial affective response will allow them to attend optionally to the infant's needs. These maternal split-second adjustments in response are too rapid to be occurring through conscious evaluation so must, at least initially, occur at an implicit level. Mothers who show unusually high or low levels of emotional arousal, and possibly associated disrupted caregiving, may therefore be experiencing abnormal emotional reactivity to infant cues, deficits in implicit emotion regulation, or a combination of both. On a neural level, these processes may reflect an imbalance between the limbic circuits (emotion reactivity) and the regulatory prefrontal circuits (emotional regulation), which may contribute to the intrusive, withdrawn or disoriented caregiving behaviors that are more frequent among mothers with psychopathology.

Reward processes include immediate hedonic responses ('liking') and approach motivation ('wanting') or learning (31). In this review we will focus on initial reward responses or the experience of pleasure when adults view or hear positive stimuli. Non-human animal and human studies on reward responsiveness suggest frontostriatal brain regions to be critically implicated, in particular the orbitofrontal cortex (OFC) (32) and the ventral striatum including the nucleus accumbens (NAcc) (33). Although the OFC generally codes hedonic signals, the medial OFC is particularly important for computing reward value while the lateral OFC makes stronger contributions to reward learning (34). In mothers, the initial experience of pleasure when exposed to their own infant's cues may promote bonding to ensure continuous engagement in caregiving. Very few studies, however, have examined neural substrates of reward-related processes among mothers who display more severely disrupted caregiving behavior.

Before reviewing the literature, it is important to mention several issues. First, emotion reactivity and implicit regulation are likely to temporally overlap. Yet, for the purpose of the

review, we will investigate whether examining these constructs individually will advance our understanding of mother–infant interaction, in particular among mothers with disrupted caregiving or psychopathology. This conceptualization is in line with models of affective chromometry and dual-process model of emotion regulation (21, 22, 28). Second, the reviewed studies were not necessarily designed to specifically assess affect and reward processes. Our interpretations therefore require further confirmation and will hopefully guide new lines of research. Third, because most imagining studies use fMRI methods, we limited our review to such methods to ensure comparability of findings. However, alternative methods using a higher temporal resolution such as electroencephalography (EEG) (e.g. 35) may provide important additional information. Finally, results of the studies to be reviewed below are summarized schematically in Table 1, in relation to findings in brain regions associated with emotion reactivity, regulation of emotion, and reward processes. Rather than providing an exhaustive review, we will present a focused summary to examine whether differences in these components may help to understand differences in caregiving behavior.

### **Maternal emotion reactivity to infants' positive and negative affect**

Affective responses to infant's signs of happiness or distress are critical to ensure the mother's *attention* to the infant's need. The amygdala is one of the regions critically implicated in reactivity to negative and positive stimuli in the environment to facilitate emotional learning (23, 24). Several studies have found increased amygdala activation in mothers in response to visual cues of their own infant versus an unfamiliar infant (36, 37). Lenzi et al. (37) further found that when mothers imitate their infants' joyful expressions, right limbic and paralimbic areas are recruited, including the amygdala and the insula, a region involved in feelings of empathy. Activation of this circuit may therefore facilitate heightened emotional responding and greater engagement with familiar infants. Interestingly, Barrett and colleagues (38) reported that mothers who experienced greater parental distress or less positive attachment in the parental role displayed reduced amygdala activation to positive faces of own infant versus unfamiliar infant. In summary, maternal amygdala response as an index of positive emotional reactivity to infant images may be an important contributor to sensitive caregiving.

However, negative facial expressions have also been shown to activate the amygdala (39), which may depend on parental experience (40). For example, parents displayed greater right amygdala activation to an unfamiliar infant's crying versus laughing, while non-parents showed greater amygdala activation to an unfamiliar infant's laughing versus crying (40). Results highlight the emotional salience of negative infant signals to parents, which would be critical to ensure the offspring's survival. In fact, Swain and colleagues (41) suggested that the experience of being a parent may alter the parent's responses so that they are more altruistic even towards unfamiliar infant stimuli.

### **Emotion reactivity: mothers with sensitive versus disrupted caregiving**

Emotion reactivity also appears to be related to the style of mother–infant attachment. Laurent and Ablow (42) found that mothers of infants who were less securely attached showed increased activation in the amygdala, parahippocampus, and right posterior insula in

response to their own baby cry compared to non-cry control sounds. Mothers of infants who were more likely to be securely attached however, showed a deactivation to their infant's cry in these regions. Similarly, Atzil and colleagues (43) found that intrusive maternal behavior (i.e. forceful guidance of the infant), assessed in infant–mother interaction, was related to greater maternal activation in the amygdala when viewing their infant in solitary play and when viewing videos of themselves interacting with their infants. Intrusive maternal behavior was also related to increased insula and temporal pole activation (auditory processing) when listening to auditory cry sounds of their own and an unfamiliar infant (44). These results may suggest that mothers who display intrusive behavior or who have less securely attached infants show an amplified reaction to emotionally salient cues of their infants, whereas mother who are less intrusive or have more secure infants are less emotionally reactive. Heightened affect in mothers may hinder their ability to act in a secure and non-intrusive manner in the face of their infants' distress.

In addition to differences in neural responses among parents with different attachment styles, maternal responses to negative infant cues seem to be further modulated by time since delivery. At 2–4 weeks post-birth, when listening to own infant versus unfamiliar infant cry, mothers showed greater amygdala and insula activation, suggesting a heightened maternal emotional response. No such differences were found at 3–4 months postpartum. Instead activation in the mPFC, a region implicated in the top-down regulation of affect, rather than in affective reactivity per se, was increased for own versus unfamiliar infant cry at 3–4 months postpartum [see (45)]. The authors theorized that a functional re-organization of responses to infant cries occurs among parents in the early postpartum period, shifting from increased emotional responding to increased regulation of emotion as they became more familiar with the infant. In a mixed group of breastfeeding and formula-feeding mothers, Kim et al. (46) found that greater activation in right amygdala and superior frontal gyrus (SFG) at 2–4 weeks postpartum was related to greater maternal sensitivity to their infants at 3–4 months postpartum. Findings suggest that *balanced* frontolimbic activation to infant stimuli in the early postpartum period may predict later maternal sensitivity. However, further confirmation is needed as Kim et al. (46) did not assess maternal sensitivity at the time of the fMRI assessment at 2–4 weeks postpartum.

In summary, the literature suggests 1) that there are individual differences in mother's amygdala responses to infant cues, 2) that insecurely attached mothers show increased amygdala reactivity compared to those with secure attachments, and 3) that emotion reactivity may be more marked early in the postpartum period. However, further studies are needed to assess whether increased amygdala reactivity interferes with mother–child interactions due to the mother's own emotional arousal. It would be particularly useful to clarify the multifaceted role of increased amygdala activation to positive (37) and to negative infant cues (40), as well as among securely and insecurely attached parents (42) or among intrusive and non-intrusive mothers (43). Further studies should compare mothers with secure and insecure attachments as well as non-parents, using positive, negative and neutral cues of own and unfamiliar infants to answer this question. Moreover, in light of the findings suggesting a shift in emotional responding during the first 6 months after birth, the timing of maternal assessments will need to be further explored and standardized.

## Maternal emotion regulation in response to infant positive and negative affect

Activation of the PFC has been suggested as a ‘top-down’ regulatory process to modulate the limbic system (i.e. amygdala) in response to emotional stimuli (27, 28). As infant distress is likely to elicit an emotional response in the mother, implicit regulation of maternal emotion may be critical in order to *act* appropriately in response to the child’s affective cues. Therefore, mothers may recruit higher-order regulatory brain regions (e.g. PFC) to regulate their own emotional responses to salient infant communications. Indeed, mothers who displayed greater attunement and responsiveness to infants’ signals during a free play interaction also exhibited increased activation in the right PFC, specifically in the frontal pole and inferior frontal gyrus (IFG) (44). When viewing videos of own versus unfamiliar infant in a separation situation, mothers recruited regions associated with emotion regulation and response inhibition (dorsal medial PFC, IFG) in addition to regions associated with processing of reward/punishment to aid in decision-making (OFC) (47). When presented with negative affective cues of own infant versus unfamiliar infant, Barrett and colleagues (38) found that mothers had greater activation in the subgenual anterior cingulate cortex (ACC), a region adjacent to the ventromedial PFC with strong connections to the limbic system. The subgenual ACC plays a key role in the autonomic and neuroendocrine arousal associated with emotional states (48) and is implicated in emotional regulation (49). In arousing caregiving situations, frontal regions may therefore play a role in modulating automatic negative emotions elicited by infant distress to ensure continued maternal engagement with the infant.

### Emotion regulation: mothers with sensitive versus disrupted caregiving

To further investigate the interaction between emotion reactivity and regulation in the processing of infant stimuli, Laurent and colleagues (50) assessed cortisol and neurobiological responses among mothers during the Strange Situation Procedure (SSP) (51) which involves brief separations that are stressful for the infant. Mother’s physiological reactivity to her infant, as measured by cortisol response in the SSP, was significantly correlated with regions implicated in emotion reactivity and regulation. Specifically, mothers who exhibited a less reactive cortisol response during the SSP showed more neural activation in response to their infant’s cry in emotional (insula) and regulatory networks (medial PFC, ACC) involved in maternal behavior (50). Thus, mothers who are less biologically stressed during difficult interactions with their infants may also have more *balanced* activation patterns across limbic and prefrontal regions. Conversely, mothers who are more biologically stressed, as indexed by a more reactive cortisol response, may be less able to activate regulatory brain regions that are important to modulating negative emotions and attending to the infant.

Finally, Kim et al. (52) investigated structural differences in gray matter volume at 2–4 weeks among mothers who reported higher maternal care in their own childhoods versus mothers who reported lower maternal care in childhood. Higher perceived maternal care in childhood was associated with larger gray matter volumes in a number of frontal and temporal regions. Further, using fMRI, higher perceived maternal care was associated with



increased activation in frontal regulatory regions and temporal regions to a standardized infant cry (unfamiliar infant) (i.e. dorsolateral PFC, middle frontal gyrus (MFG), superior temporal gyrus (STG) (52). Among mothers with higher perceived maternal care, brain regions with larger gray matter volume also showed higher functional activation compared to activation among mothers with low perceived maternal care. Together, these associations may suggest that mothers who have experienced sensitive care in childhood are able to sensitively attend to infant cues and rely on regulatory processes to modulate their own elicited distress and to facilitate appropriate responding. However, the extent to which a mother's own experiences in childhood affect the way that she responds to her own infant requires further investigation, in part due to the variety of confounding variables that may affect structural and functional brain development across the life span and in part due to the retrospective evaluation of early caregiving experiences.

In sum, research reviewed in this section emphasizes the role of regulatory functions. Although emotional responses are critical to attending to the infant, activation of regulatory circuits may allow a more balanced response that appears to play a role in sensitive caregiving. Sensitive mothers appear to be able to regulate their own initial emotional responses in the service of responding to the infant's needs without becoming disrupted by their own negative affect. A balance between frontal and limbic systems may therefore be important to facilitate sensitive maternal responding. Stressed or insecurely attached mothers appear to have less activation of prefrontal regions or ACC, possibly indicating less efficient regulation of their emotions. Although these findings are in line with research suggesting the vital role of prefrontal networks in maternal attachment behavior (47, 53–57), further research is needed to test this hypothesis, for example, by using Emotional Go-NoGo paradigms with infant cues.

### **Maternal reward responsiveness to infant positive and negative affect**

In addition to reactivity and regulation, the extent to which a mother finds the interaction with her infant *rewarding* may be important in sustaining the motivation to engage in caregiving behavior. Research to date has suggested that OFC activation may be involved in feelings of approach, affiliation, and liking (47, 53, 54, 58). Initial reward responsiveness relies on frontostriatal regions including, but not limited to, the OFC and ventral striatum (i.e. NAcc). Increased OFC and increased striatal activation to a happy face may therefore reflect a more rewarding experience that can positively reinforce caregiving behavior (59). Consistent with this hypothesis, mothers showed increased OFC activation to images of their own infant versus an unfamiliar infant (56). These mothers also self-reported more positive feelings when viewing pictures of their own versus an unfamiliar infant. Mother's subjective experience of reward and associated activation of reward-related brain regions when presented with their own infant could serve as a motivational mechanism underlying maternal attentiveness and mother-child attachment, despite experiencing distress at times when attending to the child.

Noriuchi et al. (47) further reported that increased activation in the putamen, a dorsal striatal region, to positive images of their own child was associated with self-report measures of increased positive motherly feelings toward their own versus an unfamiliar infant.

Furthermore, mothers displayed increased putamen and left substantia nigra BOLD signals to happy, smiling images of their own infant compared to negative or neutral faces (60). Interestingly, Bartels and Zeki found that maternal love and romantic love activated similar regions implicated in reward-related processes (e.g. striatum, substantia nigra), as well as other regions implicated in affect (e.g. insula, ACC), as assessed by viewing stimuli of a romantic partner and of one's own infant (53). However, the left OFC and periaqueductal gray (PAG) appeared specifically activated in maternal love but not in romantic love, suggesting a partially different mechanism for the mother-child relationship (53).

### **Reward responsiveness: mothers with sensitive versus disrupted caregiving**

While viewing videotaped infant-mother interactions, mothers who were more synchronous in interaction with their infants at 4-6 months displayed greater activation in the left nucleus accumbens, a ventral striatal region implicated in reward responsiveness or 'liking'. A similar pattern was not observed among intrusive mothers (43). Thus, this limited evidence may be interpreted that more sensitive mothers experience the infant-mother interaction as more rewarding than do more intrusive mothers. However, as current studies have not been designed to specifically assess differences in reward responses, further research is imperative. Neural responses to infant stimuli associated with more withdrawing or disoriented forms of disrupted maternal behavior (16, 61) have not been studied.

In addition to receiving dense dopaminergic projections, regions of the reward circuitry have dense concentrations of vasopressin and oxytocin receptors (62), which play important roles in reward learning and feelings of attachment, respectively. In response to infant cry stimuli among non-mothers, oxytocin administered nasally was found to reduce amygdala and to increase insula and IFG activation (63). Thus, oxytocin may be involved in the balanced regulation of intense emotional responses to negative infant stimuli and the promotion of empathic emotional responses (63). Strathearn et al. (64) found that mothers who had secure states of mind regarding their own attachment figures in childhood, as assessed on the Adult Attachment Interview (65), exhibited increased oxytocin levels, a hormone involved in attachment and bonding. In addition, when viewing happy images of their own infant, these secure mothers showed greater activation in reward-related (e.g. ventral striatum, OFC) and regulatory regions (e.g. mPFC) compared to mothers judged to have insecure/dismissing states of mind regarding their attachment relationships. In response to negative images of their own child, secure mothers also showed similar activation in reward-related regions. In contrast, insecure/dismissing mothers recruited the bilateral anterior insula. While the authors posit that this insula activation may be related to aversive emotions (64), insula activation in previous studies has been interpreted as a neural correlate of empathy (37, 52, 53, 66). Thus, insecure/dismissing mothers may experience child distress vicariously, and have fewer regulatory responses available to maintain a positive feeling toward the infant. Although consistent with an extensive literature documenting less adequate behavioral responses of dismissing mothers to infant distress (67), this hypothesis will need to be more systematically explored in future research.



## Summary of maternal fMRI reactivity, regulation, and reward responsiveness to infant cues

In the past sections, we reviewed 1) maternal fMRI responses to infant cues and 2) their association with security and sensitivity in interaction with the infant. While limited, the current body of research suggests that mothers with sensitive caregiving behavior show emotional responding to infant cues while also regulating those emotional responses, which may help to attend appropriately to infant needs. On a neural level, these processes may be represented by a functional balance between the amygdala and the medial PFC (e.g. 27, 28). Sensitive mothers are also more likely to show activation in reward-related brain regions (i.e. OFC, striatum) that are associated with more positive feelings and, thus, may increase motivation to engage in caregiving. In contrast, neural responses associated with intrusive parenting suggest both increased reactivity to infant distress and decreased affect regulation, as well as less activation of brain regions associated with reward or 'liking'. However, as few studies have explored disrupted forms of caregiving behavior (intrusive, withdrawn, disoriented), these conclusions are preliminary and point to an important frontier for future research.

### Maternal reactivity, regulation, and reward responsiveness: mothers with psychopathology

Infant–caregiver interactions may be compromised by various forms of maternal psychiatric disturbance (10, 68–70). Given the high prevalence of maternal mental health problems postpartum (71), studying disorder-specific neural responses to infant cues and how these may interfere with caregiving behavior is a pressing topic of public health significance. Similar to the previous section, we will investigate maternal responses to infant cues by specifically focusing on neural and behavioral correlates of emotion reactivity, regulation, and reward responses.

#### Maternal depression

Mothers with postpartum depression are more likely to show reduced sensitivity as well as more intrusive or withdrawn behaviors in interaction with their infants (7, 8, 44). Such patterns of interaction have been linked to negative long-term outcomes for the child's cognitive and socio-emotional development (14, 72, 73). In one study, Papousek (5) found that depressed mothers interacting with their infants was characterized by a dyadic pattern of under-involvement (i.e. less visual contact and smiling). Mothers showed a lack of positive facial expression while infants were observed to act more lethargic, with signs of distress and self-comforting behavior. Other studies have found depressed mothers to be more hostile and intrusive in interaction with their infants (7, 8).

However, few studies have examined maternal neural activation patterns among depressed mothers to infant cues. Barrett and colleagues (38) found that higher symptoms of maternal depression/anxiety were associated with decreased maternal amygdala activation in response to positive visual stimuli of their own infants compared to unfamiliar infants. Mothers who experienced low mood and high anxiety also reported more distress during parenting and described their infant's as more difficult (38). Laurent et al. (74) reported that in response to negative infant cues, depressed mothers did not exhibit differential neural activation for their

own child's cry versus the cry of an unfamiliar child or a control sound. Non-depressed mothers, however, responded with greater activation in paralimbic and limbic regions to their own infants' cry relative to other infant or control sounds (74). Together these findings suggest an overall blunted emotional response to infant cues irrespective of infant familiarity in mothers with depression compared to non-depressed mothers. It should be noted that not all research studies have consistently reported this effect. For example, Musser et al. (44) did not find differences in mothers' neural responses as a function of perinatal depression. One reason for this null finding may be that mothers in Musser's study did not necessarily meet criteria for depression at the time of the study (1518 months postpartum) but experienced a depressive episode during the perinatal period.

With respect to reward processes, Laurent and colleagues (74) found that relative to non-depressed mothers, depressed mothers lacked activation in caudate, nucleus accumbens, and medial thalamic regions to own infant cry compared to control sounds. Overall, higher levels of current depressive symptoms were associated with diminished responses to own infant cry compared to control sounds in key affective and reward-related regions (OFC, ACC, STG, ventral striatum). Together, these results suggest that 1) depressed mothers experience both blunted emotional reactivity and reduced reward-related responses to infant cues and 2) this lack of salience applies to both own and unfamiliar infants.

Converging support for this conclusion comes from work with depressed mothers by Moses-Kolko and colleagues, using negative adult faces, rather than infant faces as stimuli. In a series of studies, addressing both emotion reactivity and reward processing, they found reduced amygdala activation to negative emotional faces among mothers with more severe postpartum depression (75). In addition, mothers with postpartum depression exhibited more rapid attenuation of ventral striatal responses to monetary reward (76). Thus, both blunted emotional reactivity and diminished reward responses may be mechanisms that can impair important attachment processes among mothers with depression.

### **Maternal posttraumatic stress disorder**

In comparison to healthy mothers, mothers with a history of trauma may show less involvement and more hostile interaction with their infants (9). For example, mothers who have PTSD show impaired reading of their children's affect, less empathic responsiveness, and less availability for joint attention, particularly after a social stressor such as mother-child separation (10). Therefore, it is important to improve our understanding of the neural circuitries relevant to parenting among mothers with a history of trauma.

Among mothers with and without PTSD related to interpersonal violence (PTSD-IPV), Schechter and colleagues (77) assessed fMRI responses to videos of own versus unfamiliar children during separation or quiet play. During separation (vs. play) of their *own* children, mothers without PTSD revealed significantly greater activation in PFC (i.e. SFG) suggesting regulatory efforts during phases of their child's distress compared to PTSD-IPV mothers. However, mothers without PTSD no longer recruited regulatory regions when viewing unfamiliar children in a separation scenario, possibly showing a diminished need to regulate their emotional responses. In contrast to non-PTSD, mothers with PTSD-IPV displayed significantly greater activation in limbic and caudate regions for separation scenarios with

both own (i.e. anterior ethorinal cortex; AEC) and unfamiliar children (i.e. amygdala, AEC, perirhinal cortex). Most critically, PTSD symptom severity was correlated with hyperactivation in these fear-circuit-related regions when viewing separations (amygdala, perirhinal cortex, hippocampus), irrespective of whether the child was their own or an unfamiliar child (77). Behaviorally, mothers with PTSD were less emotionally available to their child, as observed during the reunion episodes with the child following the separation procedures (77, 78).

Thus, preliminary evidence suggests that mothers with PTSD display greater emotion reactivity, specifically greater activation in fear-response circuitry, and less activation in prefrontal regulatory regions, irrespective of the familiarity of the infant. This finding is further supported by reports of higher subjective stress levels when viewing young children during separation by mothers with PTSD-IPV relative to non-traumatized mothers. This increased emotional reactivity and difficulty in emotion regulation may, in turn, contribute to the mother's observed emotional unavailability when interacting with her child. Lastly, the role of caudate activation among PTSD mothers in response to viewing mother-child separation scenarios deserves further investigation.

Understanding the neural correlates of caregiving in PTSD mothers is especially important as children of mothers with PTSD are at risk for long-term disturbances in the regulation of their emotions, arousal and behavior (79). Furthermore the relationship between neural responses and parenting behaviors among mothers with PTSD may be promising in informing treatment interventions. For example, Schechter et al. (80) found that clinically referred mothers with PTSD-IPV often misread their children's anxious facial expressions as angry and controlling. A brief video feedback therapeutic intervention facilitated the mother's reframing of the child's affect as anxiety and helplessness. Further work assessing whether neural responses as well as behavioral responses to the child can be normalized by such interventions will be important.

### **Maternal substance use**

Given the disruptions in mother-child relationships documented in substance-using populations (11), we would expect aberrant neural responses to infant stimuli among this clinical group. Landi and colleagues (81) investigated neural correlates to infant cries of varying levels of distress and to infant faces of varying emotional expressions (happy, sad, neutral) among substance-using and non-substance-using mothers at 1-3 months postpartum.

With one minor exception, no brain regions showed greater activation in substance-using mothers compared to non-using mothers in any of the conditions displaying happy, sad or neutral faces. In contrast, non-substance-using mothers showed greater activation in a range of prefrontal regions (e.g. dorsolateral PFC/MFG, ventromedial PFC, dorsomedial PFC, IFG), limbic system regions (e.g. amygdala, parahippocampal gyrus) and visual/sensorimotor regions for happy, sad, and neutral faces compared to substance-using mothers. Activation in striatal regions was also noted for non-substance-using mothers, but only in relation to neutral faces (globus pallidus).

For cries of both low and high distress, regions involved in emotional processing (amygdala, insula, parahippocampal gyrus), prefrontal regions (MFG) and regions implicated in auditory/sensorimotor processing showed greater activation among non-using mothers than among substance-using mothers (81). As these regions comprise networks supporting emotion reactivity and regulation, substance-using mothers appear to be characterized by a hyporeactivity to visual and auditory infant cues. In addition, regions identified as more active in non-using compared to substance-using mothers overlap with regions identified as more active in healthy mothers when viewing infant stimuli (82). Thus, blunted neural activity may reduce salience of cues and contribute to the maladaptive parental responses observed among substance-using mothers.

### **Summary: reactivity, regulation, and reward responsiveness among mothers with and without psychopathology**

When exposed to own versus unfamiliar infant cues, more sensitive mothers exhibit both increased emotional reactivity and increased emotion regulation compared to less sensitive mothers. Positive infant stimuli also lead to activation of regions critically implicated in reward responses. In addition, the very limited evidence on neural differences among mothers with psychiatric illnesses suggests that different patterns of neural activation to infant stimuli may be associated with different types of parental psychopathology. In contrast to healthy mothers, mothers with depression displayed an overall flattened emotional response to infant cues (74), and also failed to show increased activation in striatal reward pathways, similar to blunted reward processing among individuals with depression more generally (83). Mothers with PTSD-IPV exhibited greater activation in fear-related circuitry, with less top-down regulation when either their own or other children were in distress (77). This pattern of response among mothers with PTSD is similar to the exaggerated amygdala and diminished medial PFC response to negative stimuli found in individuals with PTSD more generally (84, 85). Such an amplification of emotional reactivity coupled with decreased ability to regulate limbic activity may contribute to the behavioral withdrawal from the distressed infant observed among mothers with PTSD. Finally, mothers who had used substances displayed a hyporeactivity to infant affective cues compared to non-substance-using mothers at 1–3 months postpartum (81).

All of these patterns of disturbed neural responses to infant cues may hinder mothers' responsive behavior toward their infants, and thus interfere with the security of the early attachment relationship as well as with the infant's later ability to self-regulate. However, given the small number of studies examining responses to infant cues in mothers with psychiatric disorders, these preliminary conclusions will need to be confirmed by future research. In addition, more work is needed assessing whether these neural response patterns are associated with problematic caregiving.

If confirmed, results on mothers with psychopathology suggest the possibility of tailoring intervention programs to address the differential neural responses among mothers with different forms of psychopathology. For example, among parents with depression, treating anhedonia as part of treatment may increase the reward or motivational value associated with

parenting to foster more positive mother–infant engagement. Mothers with PTSD might especially benefit from interventions designed to increase their own emotional self-regulation in the face of strong emotional reactivity, in order to attend better to the child’s needs. Finally, a mother with substance use may benefit from interventions that increase her emotional responsiveness to her infant’s communications. However, more research is needed to support these tentative conclusions.

Finally, this review focused on the neural regions and processes involved in reactivity, regulation, and reward. These circuits and processes are spatially and temporally overlapping, however, making it difficult to isolate particular aspects of neural function. Thus, this framework should be understood as a first step in organizing our emerging understanding of the neural processes underlying caregiving.

## Directions for future research

Many factors influence neural responsiveness to child cues among mothers. The heterogeneity in which factors are investigated in particular studies complicate comparisons of results across studies. Several factors seem particularly important to address in future designs:

1. maternal neural responses to their own versus unfamiliar infant cries seem to be modulated by time since delivery (45), suggesting a functional re-organization of sensitivity to infant cries in parents in the months after birth, with greater emerging regulation over time;
2. the type of stimulus plays a critical role (own child vs. other child vs. white noise). Stimuli derived from a mother’s own child have been shown to be more salient to mothers (44) but are not consistently used across studies (e.g. 81);
3. whether mothers are first-time mothers should be assessed in relation to neural response patterns, as parity effects have been prominent in animal studies (e.g. 86, 87);
4. the level of distress experienced by the child may affect the salience of the stimulus. Some (e.g. 59, 81) but not all studies have considered the effect of the level of the child’s distress on the parent’s neural responses; and
5. studies of mothers with psychiatric disorders often have difficulty in matching case and control groups on critical factors such as socioeconomic status (81) and comorbid psychiatric disorders (77). Because socioeconomic status is a potent variable affecting many aspects of parenting, controls for socioeconomic status are important to include in future neuroimaging studies. In addition, comorbidity among psychiatric disorders constitutes a challenge for future research attempting to identify disorder-specific neural correlates and their associated patterns of parenting.

Beyond these specific methodological issues, however, the most important challenge for future research is to relate patterns of parental neural response to patterns of observed parent–infant interaction and attachment. Without associated tasks assessing multiple

dimensions of parent–infant interaction, it becomes quite speculative to link patterns of parental neural responses to their implications for parenting and infant development. Well-designed studies are needed investigating whether neural responses associated with emotion reactivity, regulation, and reward are useful in understanding disturbances in caregiving behavior.

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Table 1.

Summary of reviewed findings

Author, Year	Design	Emotion reactivity	Emotion regulation	Reward processes	Key findings
<b>Healthy mothers</b>					
Aziz et al. (43)	fMRI: Own and unfamiliar infant videos during solitary and mother-infant play <i>Mother-infant interaction</i> : Coded for synchronous (S) vs. intrusive style (I), oxytocin (OT) assessment	I > S: (+) right amygdala	I > S: (-) dmPFC	S > I: (+) left nucleus accumbens	Synchronous maternal care was associated with activation in reward-related regions compared to intrusive mothers who showed higher emotion reactivity. Absent dorsal mPFC activation for the intrusive group may point to insufficient behavioral inhibition associated with intrusive care giving.
Barrett et al. (38)	Infant pictures: Own (O) and unfamiliar (U) faces with positive (P) and negative (N) expressions	OP > UP: (+) amygdala OP > ON: (+) insula	ON > UN: (+) subgenual ACC	ON > UN: (+) ventral putamen OP > ON: (+) striatum	Mothers recruit the amygdala when viewing OP compared to UP infants. These activations correlated positively with maternal feelings of attachment.
Bartels & Zeki (53)	Comparison of pictures: Own and familiar child, adult best friend and acquaintance Own vs. familiar child compared to romantic love data (53)	Overlap with romantic: (+) insula, posterior cingulate gyrus	Overlap with romantic: (-) mPFC	Overlap with romantic: (+) striatum, substantia nigra <i>Maternal specific</i> : (+) OFC, PAG	Maternal love overlaps with romantic love in affective and reward-related regions. Maternal love uniquely activates the OFC and PAG.
Kim et al. (87)	fMRI: Structural MRI at 2–4 weeks (Time 1) and 3–4 months postpartum (Time 2) Self-report of parenting experience and perception of her infant at 2–4 weeks postpartum	Positive perception of infant at Time 1: increased gray matter in amygdala and hypothalamus at Time 2	Time 1 > Time 2: increased gray matter in superior, middle and inferior PFC, insula	Positive perception of infant at Time 1: increased gray matter in substantia nigra	From 2–4 weeks to 3–4 months postpartum, mothers showed increased gray matter in regulatory circuitry. A mother's positive perception of her infant at 2–4 weeks predicted the degree of gray matter change in emotional and reward related brain regions at 3–4 months.
Kim et al. (52)	Perceived maternal care in mothers own childhood (PMC). Structural MRI and fMRI with exposure to unfamiliar infant cry vs. control noise	High PMC: increased gray matter in frontal gyri, (+) dlPFC, MFG			High PMC was related to increased gray matter and increased functional responses in frontal brain regions compared to low PMC. A mother's own PMC may affect the way she responds to infant stimuli.
Kim et al. (46)	Breastfeeding (BF) vs. formula feeding (FF) mothers 2–4 weeks postpartum: fMRI during exposure to own vs. other infant cry 3–4 months postpartum: Interaction coded for maternal sensitivity	BF > FF to own cry: (+) insula, amygdala	BF > FF to own cry: (+) SFG, left IFG	BF > FF to own cry: (+) striatum	Breastfeeding mothers showed increased activation in affective and reward-related regions to own infant cry. Increased activation at 2–4 weeks postpartum was associated with more sensitive care giving at 3–4 months postpartum.
Laurent & Ablow (42)	fMRI: Own (O) and unfamiliar (U) infant cry and control sound (C) <i>Strange Situation</i> : Interaction coded for attachment and attachment related behaviors	Greater likelihood of insecure infants (O vs. C): (+) parahippocampal gyrus extending to ventral amygdala, right posterior insula <i>Greater likelihood of secure infants</i> : (-) parahippocampal gyrus extending to ventral amygdala, right posterior insula	Mothers of infants with more insecure behaviors (O vs. C): (-) left OFC, dlPFC, right middle frontal gyrus, subgenual ACC		Mothers of infants with more insecure behavior showed greater emotion reactivity and less recruitment of prefrontal regulatory areas to their own infant's cry. Mothers of infants more likely to be secure showed decreased activation to infant cry in regions implicated in emotional response.

Author, Year	Design	Emotion reactivity	Emotion regulation	Reward processes	Key findings
Laurent et al. (50)	fMRI: Own (O) and unfamiliar (U) infant cry, control sound <i>Strange Situation</i> : cortisol collection, HPA reactivity measured by trajectory curvature	Less overall HPA reaction: (+) insula	Less HPA reaction: (+) ACC, mPFC	Less overall HPA reaction: (+) PAG, striatum, thalamus, lateral OFC	Mothers who had a less reactive HPA profile over the course of the strange situation had increased activity in emotional, regulatory and reward regions in response to their own baby's cry compared to more HPA reactive mothers. Mothers who are less stressed while interacting with their distressed child may be better able to respond appropriately.
Leibenluft et al. (36)	fMRI: Pictures of own (O), familiar (F), and unfamiliar (U) children, and unfamiliar adults (A)	O > F: (+) right amygdala, left anterior insula F > U: (+) left insula, (-) left amygdala U > A: (+) left insula	O > F: (+) dlPFC		When mothers view pictures of their own child, they show increased emotion reactivity and regulation compared to other familiar cues.
Lenzi et al. (37)	fMRI: Observing and imitating pictures of own (O) and unfamiliar (U) children's emotions (joy, distress, ambiguous, neutral)	Viewing O > U: (+) insula, amygdala Joy vs. other imitation: (+) insula, amygdala		Joy > other imitation: (+) basal ganglia	When viewing emotional expressions of their own vs. unfamiliar child, and when imitating joyous facial expressions mothers have increased responses in affective and reward regions.
Lorberbaum et al. (54)	fMRI: Unfamiliar infant cries, control sound, and rest condition	Cry > rest: (+) right amygdala Control minus rest: (+) right amygdala	Cry > control: (+) mPFC	Cry > control: (+) caudate, putamen, nucleus accumbens, right OFC, substantia nigra	Mothers have increased activity in emotional, regulatory and reward regions to cry stimuli compared to control noise and rest. These activations were stronger in the right hemisphere.
Nitschke et al. (56)	fMRI: Pictures of own (O) and unfamiliar (U) infant and familiar and unfamiliar adults. Self-report of maternal mood			O > U infant: (+) bilateral OFC	Mothers had stronger OFC activation (reward liking) when viewing pictures of their own infant compared to an unfamiliar infant. These activations correlated with reported maternal positive mood.
Noriuchi et al. (47)	fMRI: Video clips of own (O) and unfamiliar (U) infant in play situation (PS) and separation situation (SS). Self-report mood while watching video clips	O > U: (+) anterior insula	O > U: (+) dmPFC SS > PS with O: (+) dmPFC, ACC, left PFC	O > U: (+) right OFC, dorsal and ventrolateral putamen, PAG SS > PS with O: (+) dorsal OFC, caudate, thalamus, substantia nigra	Mothers showed more activation in regulatory regions when viewing their infants in the SS compared to the PS. Stronger emotional responses were noted when mothers viewed video clips of their own compared to other infants.
Ranote et al. (57)	fMRI: Video clips of 'content' own (O) and unfamiliar (U) infant and neutral (non-infant)	O > U: (+) left amygdala, anterior temporal cortex	U > O: (+) right dlPFC, right mPFC,	U > O: Bilateral lateral OFC	Mothers showed increased amygdala and temporal cortex activation when viewing their own compared to unfamiliar infants. Increased PFC activation when viewing unfamiliar infants may suggest mothers recruit cognitive control to restrain tendencies to interact with the unfamiliar infant.
Riem et al. (63)	fMRI: Randomized control trial of oxytocin (OT) nasal spray to non-mothers while listening to infant cry and control sounds	Placebo cry > control: (+) right amygdala OT cry vs. control: (+) insula, IFG (-) right amygdala			When administered to non-mothers listening to infant cry, oxytocin decreased activation in the right amygdala.
Seifritz et al. (40)	Parents (P) of young children and non-parents (NP)	P > NP to cry: (+) amygdala, insula,	Women > Men: (-) right ACC, right mPFC		Parents had greater activation to infant cry in affective and regulatory brain regions compared to laughter. Non-parents had greater activation in



Author, Year	Design	Emotion reactivity	Emotion regulation	Reward processes	Key findings
Strathearn et al. (60)	<i>fMRI</i> : Unfamiliar infant crying and laughing and control stimulus	<i>NP &gt; P to laugh</i> : (+) amygdala, insula	<i>P &gt; NP to cry</i> : (+) middle cingulate cortex, ventral PFC, >TPJ <i>NP &gt; P to laugh</i> : (+) middle cingulate cortex, ventral PFC, TPJ	<i>O &gt; U</i> : striatum, VTA, substantia nigra <i>O happy &gt; U happy</i> : (+) bilateral putamen, left substantia nigra, right thalamus	these same regions in response to infant laughter compared to cry. Functional changes may take place in these brain regions in the transition into parenthood.
Strathearn et al. (64)	<i>fMRI</i> : Pictures of own (O) and unfamiliar (U) infants with happy, neutral and sad expressions <i>Attachment</i> : Secure vs. insecure mothers (attachment in own childhood)	<i>O &gt; U</i> : (+) insula, lateral amygdala <i>O happy &gt; U happy</i> : (+) left lateral superior amygdala	<i>Secure</i> : <i>O &gt; U</i> : (+) bilateral lateral PFC, left mPFC <i>O happy</i> : secure vs. insecure mothers: (+) mPFC <i>O happy</i> : insecure vs. secure mothers: (+) dlPFC <i>O sad</i> : insecure vs. secure mothers: (+) dlPFC	<i>O happy</i> : secure > insecure mothers: (+) ventral striatum, OFC <i>O sad</i> : secure > insecure mothers: (+) ventral striatum	Mothers have increased activation in reward regions when viewing their own compared to unfamiliar infants. Viewing happy faces activates these regions more than viewing neutral or sad faces.  Secure mothers have increased activations in reward related brain regions when viewing happy and sad faces of their own infant. Insecure/dismissive mothers had increased insula activation to their infant's sad face. Secure mothers had higher oxytocin levels during infant interaction than insecure/dismissive mothers.
<b>Mothers with psychopathology</b>					
Landi et al. (81)	<i>Substance use</i> : Self-report and urine toxicology of substance use during pregnancy and/or postpartum (SU); non substance-using mothers (NU) <i>Stimuli</i> : Infant cry of high and low distress, neutral tone; happy, sad and neutral faces	<i>NU &gt; SU for sad faces</i> : (+) right amygdala, para-hippocampalgyrus <i>NU &gt; SU for neutral faces</i> : (+) right amygdala, para-hippocampalgyrus	<i>NU &gt; SU for happy faces</i> : (+) vmPFC, right dlPFC/mFG, dmPFC <i>NU &gt; SU for sad faces</i> : (+) dlPFC/mFG, right IFG, medial OFC, middle STG	<i>NU &gt; SU for neutral faces</i> : (+) globus pallidus	Reduced activation for substance-using mothers relative to non-using mothers for visual and auditory infant-related stimuli. Outcomes suggest decreased emotion reactivity associated with substance use in mothers.
Laurent & Ablow (74)	<i>Depression</i> : Mothers with depression during perinatal period (MDD) vs. non-depressed mothers (ND).	<i>NU &gt; SU for low distress cries</i> : (+) insula, thalamus, bilateral amygdala/ para-hippocampal gyrus <i>NU &gt; SU for high distress cries</i> : (+) insula, bilateral amygdala/ para-hippocampal gyrus	<i>NU &gt; SU for neutral faces</i> : (+) SFG, vmPFC, dlPFC, right IFG <i>NU &gt; SU for low distress cries</i> : (+) MFG <i>NU &gt; SU for high distress cries</i> : (+) left SFG/MFG	<i>NU &gt; SU for neutral faces</i> : (+) globus pallidus	Reduced activation for substance-using mothers relative to non-using mothers for visual and auditory infant-related stimuli. Outcomes suggest decreased emotion reactivity associated with substance use in mothers.
Laurent & Ablow (74)	<i>Depression</i> : Mothers with depression during perinatal period (MDD) vs. non-depressed mothers (ND).	<i>OD &gt; C only in ND mothers</i> : (+) insula	<i>OD &gt; C only in ND mothers</i> : (+) dmPFC	<i>OD &gt; C only in ND mothers</i> : (+) striatum, thalamus, midbrain	Depressed mothers did not show increased response to own infant cry compared to unfamiliar infant or control sound. Depressed

Author, Year	Design	Emotion reactivity	Emotion regulation	Reward processes	Key findings
Musser et al. (44)	<i>Auditory infant cues:</i> Own infant in distress (OD), unfamiliar infant in distress (UD), control sounds (C)  <i>Depression:</i> Mothers with depression during perinatal period (MDD) vs. non-depressed mothers. <i>Interaction:</i> Mother-infant observations coded on sensitivity at 18 months postpartum. <i>fMRI:</i> own (O) and unfamiliar infant cries (U), control sounds	<i>O &gt; U in intrusive mothers:</i> (+) left insula	<i>O &gt; U in sensitive mothers:</i> (+) right PFC (frontal pole, IFG)	<i>ND &gt; MDD for OD</i> >C: (+) striatum, thalamus	mothers showed diminished responses to own infant compared to non-depressed mothers.  No group differences in neural responses when comparing depressed vs. nondepressed mothers. Increased PFC activation in sensitive mothers suggest ability to regulate own response to ensure sensitive caregiving. Intrusive behavior was associated with greater insula (affiliation) and temporal pole (auditory processing) activation.
Schechter et al. (77)	<i>PTSD related to interpersonal violence (PTSD-IPV):</i> <i>Videotaped interaction:</i> Separation (S) and Play (P) with own infant, unfamiliar boy, unfamiliar girl in mothers with and without PTSD-IPV	<i>PTSD &gt; non-PTSD to O:</i> (+) AEC, left caudate <i>S &gt; P for U in PTSD &gt; non-PTSD:</i> (+) right amygdala, AEC, perirhinal cortex, left caudate <i>S &gt; P for O and U in PTSD vs. non-PTSD:</i> (+) left insula	<i>non-PTSD &gt; PTSD to O:</i> (+) SFG <i>PTSD vs. non-PTSD to U:</i> (+) MFG		During separation, PTSD-IPV mothers activated fear-circuit-related regions to own and unfamiliar infants in separation condition. Mother without PTSD-IPV showed greater activation in regulatory regions to viewing own infant but not to viewing an unfamiliar infant during the separation episode. PTSD symptom severity was correlated with hyperactivation in fear-circuit-related regions when viewing separations irrespective of whether child was own or unfamiliar.

ACC = Anterior cingulate cortex, AEC = anterior ethorhinal cortex, dACC = dorsalanterior cingulate cortex, dmPFC = dorsal medial prefrontal cortex, IFG = inferior frontal gyrus, mPFC = medial prefrontal cortex, MFG = middle frontal gyrus, STG = superior temporal gyrus, STS = superior temporal sulcus, TPJ = temporoparietal junction, PFC = prefrontal cortex, PAG = periaqueductal gray, OFC = orbital frontal cortex, vmPFC = ventral medial PFC, VTA = ventral tegmental area. (+) indicates regions with increased functional activation; (-) indicates regions with decreased functional activation.