

Annual Research Review: All mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences

Jennifer Barrett and Alison S. Fleming

Department of Psychology, University of Toronto at Mississauga, Mississauga, Ontario, Canada

Quality of mothering relies on the integrity of multiple physiological and behavioral systems and on two maternal factors, one proximal and one distal, that have a great impact on how a mother mothers: postpartum depression and early experiences. To mother appropriately requires the action of systems that regulate sensation, perception, affect, reward, executive function, motor output and learning. When a mother is at risk to engage in less than optimal mothering, such as when she is depressed or has experienced adversity in childhood, the function of many or all of maternal and related systems may be affected. In this paper, we will review what is currently known about the biological basis of mothering, with attention to literature on hormones but with a particular focus on recent advances in the fields of functional neuroimaging. Instead of discussing strictly ‘maternal’ brain imaging studies, we instead use a systems approach to survey important findings relevant to brain systems integral to and/or strongly related to the mothering experience: (a) social behavior; (b) reward and affect; (c) executive function; and (d) maternal behavior. We find that there are many commonalities in terms of the brain regions identified across these systems and, as we would expect, all are sensitive to the influence of, or function differently in the context of, depression and adverse early experience. It is likely that the similarity and cross-talk between maternal, affect and stress systems, observed behaviorally, hormonally and in the context of brain function, allows for mood disturbance and early adverse experiences to have a significant impact on the quality of mothering and the motivation to mother. **Keywords:** Adversity, maternal depression, brain imaging, parenting, mothers.

The interaction between a mother and her infant can be like a dance. There are routines, standards and missteps, there is give and take, there is unparalleled intimacy, there are often vast differences in skill level and motivation, there is learning. A mother must learn to be an adept partner, being sensitive to the needs of her offspring while ultimately guiding the quality and nature of care to ensure normal growth and development. This dance can be beautiful, it can be tender, it can be awkward, it can be difficult. And sometimes it just does not occur!

Romanticism aside, the mother–offspring dance is influenced by and interacts with many factors, including mothers’ physiology, cultural and family context, maternal cognitions, maternal affect and stress and the early environment, notably a mother’s own early experiences in her family of origin. Biological influences certainly include how mothers’ brains are organized and how genes and environment interact in brain development. It is believed that over the course of pregnancy and through the postpartum period, changes in the levels of certain hormones likely ‘activate’ or affect key brain regions to ensure that the mother is especially attracted to her baby, that she is attentive and sensitive to her

baby’s needs, that she learns from her experiences and that she behaves appropriately.

In humans, across cultures there exist as many differences as similarities in the ways that mothers interact with their infants (Leiderman & Leiderman, 1977). In some cultures the infants are carried in cradleboards on the mothers’ backs; in others they are carried in a pouch or sling on the mothers’ ventrum; in many Western cultures, especially if the terrain is smooth, infants are transported in strollers or perambulators (Anisfeld, Casper, Nozyce, & Cunningham, 1990; Chisholm, 1978). Customs relating to sleeping also vary across cultures, from swaddling, sleeping in the mother’s bed, to sleeping in a cot next to the mother, to sleeping away from the mother in another room (Van Sleuwen et al., 2007; Thoman, 2006). Mothers also exhibit a range of different kinds of communicative responses to their infants: some look at them directly while others gaze avert (Brazelton, 1977); some keep their babies unclothed and stroke their bodies; others swaddle them instead (see Corter & Fleming, 2002). Some talk or sing to their babies; others do not (Tronick, 1987). Soothing methods, for example pacifier use or use of specific herbs or teas, can greatly vary by culture (Abdulrazzaq, Kendi, & Nagelkerke, 2009). More subtly, within a culture mothers show large variations in the postpartum development of

Conflict of interest statement: No conflicts declared.

© 2010 The Authors. *Journal of Child Psychology and Psychiatry*

© 2010 Association for Child and Adolescent Mental Health.

Published by Blackwell Publishing, 9600 Garsington Road, Oxford OX4 2DQ, UK and 350 Main St, Malden, MA 02148, USA

nurturant feelings, from minutes to months (Leifer, 1980; Moss & Jones, 1977; Robson, 1967; Robson & Kumar, 1980; Trevathan, 1983), and, once 'attached' or emotionally committed, in the intensity with which they exhibit different caregiving behaviors. Within all cultures most mothers are motivated to provide warmth, shelter, and food to the infant while in all cultures there are mothers who neglect or even abuse their infants (see Corter & Fleming, 2002; Hrdy, 2005, 2009).

Despite these differences, in most cultures mothers nurse their infants, although there are some mothers in each that may also bottle-feed (Kannan, Carruth, & Skinner, 2004; Pak-Gorstein, Hak, & Graham, 2009; Thulier, 2009). In many different cultures, mothers engage in a form of expression called 'motherese', where the mother talks to the infant in a high prolonged pitch and sings with a characteristic cadence and rhythm (Trehub, Unyk, & Trainor, 1993). In most cultures mothers provide kinesthetic stimulation by stroking and rocking the baby and respond contingently to infant cries and other indices of distress, often by vocalizing 'in response' (Ainsworth, Bell, & Stayton, 1974; Corter & Fleming, 2002; Pederson et al., 1990). Here we will not address the issue of cross-cultural differences, important though they are (Cote & Bornstein, 2009; Güngör & Bornstein, in press). Instead we focus on the cross-cultural similarities and focus most discussion on studies that describe mothers from Western and industrialized societies, where most of the psychobiological research has occurred (see the work of Marc Bornstein for a program of research well suited to a cross-cultural analysis).

For this paper our primary focus is reflected in the idea that mothering is not unitary, but is instead complex, and comprised of many behavioral propensities that are mediated, moderated, and regulated by multiple physiological and brain systems. To engage in mothering behavior, mothers have to be sensitive to infant cues and select those cues for processing, utilizing multiple sensory and perceptual modalities; the cues must be attractive and salient for the mother, recruiting reward and approach systems. Mothers must be emotionally prepared and positively motivated to engage socially with the infant, depending on systems regulating affect. They must selectively attend to the offspring in the context of competing stimuli, enacted through systems that regulate attention; and they must be restrained and consistent in their responsiveness, depending on systems that regulate impulsivity. Finally, mothers gain through experiences, acquired both early in life and with young as juveniles and in adulthood. These experiences are acquired, consolidated, and stored as motor or sensory memories and are based on extensive brain plasticity.

Thus, to mother appropriately requires the action of multiple systems in the domains of sensation, perception, affect, reward, executive function, motor

output and learning. When a mother is at risk to engage in less than optimal mothering, such as when she is depressed or has experienced adversity in childhood, the function of many or all of these systems may be affected. In this paper, we will use a systems approach to review and critique what is currently known about the biological basis of mothering, with a particular focus on recent advances in the field of functional neuroimaging. We will often combine information from the animal world with the human. We will briefly review what has informed knowledge of the neurobiology of mothering up until this point (hormones). Finally, whenever possible, we will try to put these basic mechanisms into the context of important individual differences related to maternal psychopathology (depression) and early adversity.

I. Maternal behavior is affected by mothers' cognitions, executive function, and theory of mind

Overview

How mothers relate to their infants is affected by multiple psychological propensities, including her cognitive style and her affective state. In this first section we discuss individual differences related to cognitive functions: functions that are thought to provide an important foundation for quality of mothering and maternal behavior and are also, in many cases, known to interact with affect/mood and early experiences. Processes such as cognitive flexibility, working memory and attentional control are fundamental components of mothering and key to maternal sensitivity. A mother must have the attentional command to focus on her infant which allows her to be sensitive to infant needs, that is, to respond contingently, appropriately and in a timely manner. She must also have the cognitive flexibility to switch her attention efficiently across many situational demands, in highly stimulating environments. She must also maintain and manipulate information in her working memory to plan and guide mother-infant interaction and infant care. In addition, the application of the concept of Theory of Mind (ToM) to mothering, where the strongly related concept of 'mind-mindedness' has also been examined (see Meins et al., 2003), is relatively new and exciting. Theory of Mind, which, among other things, is a theory relevant to social cognition and describes how we understand the intentions and emotions of others, has obvious implications for mothering, where correctly identifying and responding to infant signals or intentions is key.

Executive function

Work in the rat has demonstrated that the integrity of maternal behavior is linked to executive functions

such as attentional set-shifting and prepulse inhibition (e.g., Afonso, Sison, Lovic, & Fleming, 2007; Lovic & Fleming, 2004). In terms of human mothers, recent work in our lab by Andrea Gonzalez examined neuropsychological and physiological factors as intervening variables between maternal retrospective reports of early adversity (childhood maltreatment and consistency of care) and current parental ability (maternal sensitivity) in a sample of 90 mothers. In this work, Gonzalez proposed and tested a model linking maternal early adversity to maternal sensitivity through the hypothalamic-pituitary-adrenal (HPA) axis and executive functions (e.g., attention). It is of note that the latter was predicted to be important for maternal behavior and thought to be mediated by HPA axis function. A composite maternal sensitivity score was correlated with measures of attentional set-shifting, spatial working memory, and a sustained attention measure; results revealed that maternal sensitivity was significantly related to both set-shifting and spatial-working memory. Importantly, path analyses revealed that maternal early adversity was indirectly related to maternal sensitivity via two pathways: (1) early adversity-HPA function-maternal sensitivity; and (2) early adversity-HPA function-executive function-maternal sensitivity. In this population of mothers, the mothers' affective state did not enter into the model. Of interest to us is the possibility that in a population of mothers where postpartum depression is high, early experience effects may also affect cognition and maternal sensitivity by acting to alter mothers' affective state. However, the importance of HPA function in mothering will be described in detail, in the section to follow.

Atkinson and colleagues investigated mother-infant interaction, attachment and selective attention using the emotional Stroop task and found that mothers with a classification of disorganized attachment responded more slowly to negative attachment words and that the speed of response to such stimuli was correlated with the number of times the mother-infant dyad was labeled as disorganized (Atkinson et al., 2009). The authors interpret these findings in the context of parallel processing and distributed semantic (neural) networks, where attachment stimuli (i.e., infant) are connected to negative associations (e.g., threat, loss). Such mechanisms may contribute to ongoing cognitive (attentional) interference/difficulties during mother-infant interactions (Atkinson et al., 2009). The results of these studies underscore the complexity of the mechanisms underlying mothering and how a multi-system approach is important when trying to understand individual differences that may contribute to maladaptive mothering styles.

In terms of individual differences in mothering and executive functions, in rats maternal deprivation is related to deficits in executive function-processes such as prepulse inhibition (PPI) and set-shifting

(Burton, Lovic, & Fleming, 2006; Garner, Wood, Pantelis, & van den Buuse, 2007; Lovic & Fleming, 2004). Many studies of early adversity in children have found a relationship between abuse or neglect and executive function (Bos, Fox, Zeanah, & Nelson, 2009; De Bellis, 2005; Kreppner, O'Connor, & Rutter, 2001; Pears & Fisher, 2005). Bos and colleagues examined executive function (CANTAB) in children with a history of early deprivation as a result of institutionalization and found that early adversity is related to performance deficits on tasks involving planning and working memory (Bos et al., 2009). Early adversity as a result of familial violence has also been linked to deficits in a broad range of executive functions, including problem solving, working memory, inhibition and attentional control (Fishbein et al., 2009; Nolin & Ethier, 2007; Pears, Kim, & Fisher, 2008). Although we may expect that observed early adversity-related deficits in executive function may persist into adulthood, less is known about the general influence of early adversity on executive function in adults. In the context of mood, deficits in executive function have also been widely linked to major depression and other affective disorders (Fossati, Ergis, & Allilaire, 2001). Although results have been mixed (see Rogers et al., 2004), individuals with depression have been shown to have difficulties with executive functions such as working memory (Elliott et al., 1996; Kaneda, 2009; Sweeney, Kmiec, & Kupfer, 2000), set-shifting (Grant, Thase, & Sweeney, 2001; Moritz et al., 2002) and attentional control (Nakano et al., 2008).

Theory of Mind

Maternal mind-mindedness reflects the tendency to treat one's infant as an autonomous human being with complex desires and intentions and not just basic or reflexive organismic needs, as well as the ability to correctly interpret infants' implicit and explicit signals (Meins et al., 2003). Interestingly, this trait or tendency has been identified across the perinatal period, even before the infant is born, with mothers more likely to comment on the 'personality' of the fetus exhibiting more appropriate comments regarding the infant's internal state during mother-infant interaction at six months postpartum (Arnott & Meins, 2007). Individual differences in mind-mindedness have been associated with maternal sensitivity. The work of Meins and colleagues (1998, 2001) has demonstrated that more securely attached mothers are more likely than insecurely attached mothers to have high mind-mindedness and focus on their children's mental or cognitive attributes, rather than their physical appearance or behavioral tendencies. More recently, Laranjo, Bernier, and Meins (2008) examined the relationship between maternal sensitivity, maternal mind-mindedness and infant attachment: 50 mother-infant dyads were assessed at two time points (15 and 18 months).

Results revealed that sensitivity, attachment, and mind-mindedness were all positively interrelated. In addition, the relationship between mind-mindedness and attachment was partly mediated by maternal sensitivity, a finding that was thought to support the notion that mind-mindedness is a prerequisite for maternal sensitivity, and that the correct interpretation of infant cues is fundamental to the generation of an appropriate response to such cues (Laranjo et al., 2008).

Interestingly, one individual difference that has been associated with Theory of Mind abilities is non-postpartum depression. Theory of Mind deficits have been found in remitted depressed patients and been demonstrated to be risk factors for depression relapse (Inoue, Tonooka, Yamada, & Kanba, 2004; Inoue, Yamada, & Kanba, 2006). In the context of depression, Theory of Mind deficits have been associated with impaired social cognition and cognitive distortions regarding the state of mind of others. Such impairments in social functioning may contribute to or help perpetuate the biased, negative thinking and false beliefs that often characterize depressive episodes (Sheline et al., 2009). Relatedly, one may expect that infant-related social cognition deficits related to Theory of Mind may play a strong role in depression during the postpartum period, where depressed mothers may be more likely to incorrectly assess the intentions of their infants and be biased toward more negative assessment (e.g., my baby is crying because she hates me).

II. Maternal behavior is affected by concurrent mood or depression

Overview

One of the most profound experiences a woman can have is giving birth to a new baby. She experiences intense emotions involving both extreme elation and happy feelings mixed with mild distress, lability, and tearfulness. Rapid changes in affect and extremes in affect intensity are very common and may function to heighten mothers' earliest impressions and experiences of the baby. Likely hormonally mediated, the first postpartum week is for most women an exciting and positive experience and one that maps on to many changes in mothers' awareness of their new role and the experience of 'falling-in-love' with the baby, with all the anxiety and happiness that that experience normally entails. Fleming and colleagues describe the development of these strong positive feelings of nurturance – and the associated anxiety – as they occur across pregnancy and through the first postpartum year (Fleming et al., 1997a).

In contrast to these positive feelings are the more negative feelings experienced during the first postpartum months by a substantial number of women (Friedman & Resnick, 2009; Gale & Harlow, 2003; Marcus, 2009). Although this dysphoria or

depression usually remits by 6 months postpartum, it is a source of considerable distress for the mother and her family. A great challenge of any type of depression experienced in the postpartum period is that it is in direct conflict with societal and often self-expectations of what being a new mother should and will feel like. The truth is, the early postpartum period is a time of upheaval in the physiology and psychology of the mother, when in a short time she evolves from being a pregnant woman to the caregiver of a newborn, and this change comes with new and considerable responsibilities. Although the precise reasons for it are unclear, mood disturbances during this time are incredibly common and many new mothers feel depressed at some point after the birth of their infants (Friedman & Resnick, 2009; Marcus, 2009; Moses-Kolko & Roth, 2004). Mild depressed mood, often termed 'baby blues', is experienced by up to 85% of mothers and typically resolves without treatment by the end of the first postpartum month (Buist, 2006; O'Hara, Zekoski, Philipps, & Wright, 1990).

Postpartum depression

In some women, mood disturbance may persist beyond the initial postpartum period, leading to more serious postpartum depression. Epidemiologic studies have found that up to 20% of women exhibit symptoms of depression in the first weeks following delivery (Gavin et al., 2005; Marcus, 2009), that the rise in incidence is within 30 days post-partum but persists for up to two years, and that the great majority of these depressive episodes resolve spontaneously within six months to a year (Cooper & Murray, 1995; Cox, Murray, & Chapman, 1993). The symptom profile of postpartum depression, which includes sad mood, restlessness/agitation, and impaired concentration, resembles that of a major depressive episode experienced at other times in life, but it is unique in its timing and usually involves the mother–baby dyad and in most cases affects the entire family unit. Interestingly, there is also some suggestion that greater psychomotor disturbance may distinguish postpartum from non-postpartum depression (Bernstein et al., 2008). As with depression outside of the perinatal period, postpartum depression often co-occurs with other psychiatric disorders, the most common being generalized anxiety disorder, obsessive-compulsive disorder, social phobia and agoraphobia (Figueira, Fernandes Malloy-Diniz, Aurélio Romano-Silva, Silva Neves, & Corrêa, 2009). In some rare cases, postpartum depression has been linked to suicidality and filicide (Kauppi, Kumpulainen, Vanamo, Merikanto, & Karkola, 2008; Paris, Bolton, & Weinberg, 2009). Alarming studies have also shown that as many as 50% of postpartum depression cases are undiagnosed (Chaudron et al., 2005; Murray, Woolgar, Murray, & Cooper, 2003), and reasons for this

statistic include lack of attention on the mental health of the mother by health care providers as well as under-reporting of symptoms by the mother herself. Many factors have been found to influence or mediate mothers' vulnerability to becoming depressed in the postpartum period, including: (1) factors related to childbirth and childcare such as sleep patterns, type of delivery and lack of social support; and (2) non-specific factors such as history of depression outside of the perinatal period, seasonal mood fluctuations, socioeconomic status, lack of social support, stressful recent life events and marital conflict (Boyce & Todd, 1992; Goyal, Gay, & Lee, 2009; Koo, Lynch, & Cooper, 2003; Panthangi, West, Savoy-Moore, Geeta, & Reickert, 2009; Vik et al., 2009; Xie, He, Koszycki, Walker, & Wen, 2009).

Mothering and maternal mood

Mothers with postpartum depression tend to be more intrusive and irritated, respond less sensitively, contingently and more negatively to their infants and demonstrate disrupted patterns of communication compared with mothers without postpartum depression (Beebe et al., 2008; Cohn, Campbell, Matias, & Hopkins, 1990; Field, Healy, Goldstein, & Guthertz 1990; Field et al., 1985; Fleming, Ruble, Flett, & Shaul, 1988; Paris et al., 2009; Righetti-Veltema, Conne-Perréard, Bousquet, & Manzano, 2002, for a review see Field, 2009). When observed later in the postpartum period, depressed dyads (i.e., mother-baby pairs) exhibit reduced mutual attentiveness, vocal and visual communications, touching interactions or smiling compared with non-postpartum depression dyads (Field et al., 1990; Fleming et al., 1988; Righetti-Veltema et al., 2002). For example, a recent study by Field and colleagues (2007) examined mother-infant interaction in depressed and non-depressed dyads using the still-face paradigm. Infants were approximately 4 months old at the time of testing. One of the authors' main findings, in terms of maternal responsiveness, was that the mothers with postpartum depression were less interactive with their infants at baseline (less smiling and moving of infant limbs) as well as in the still-face reunion period (less smiling, touching and moving of infant limbs). The latter finding is especially telling as a main feature of the reunion period of the still-face paradigm is to attempt to reinstate more positive interaction or regulate the emotion of the infant. It is of note that more practical, but equally important, maternal activities are also influenced by depression, including breastfeeding, bedtime routines, medical care and safety practices (reviewed in Field, 2009).

Postpartum depression also has deleterious implications for the cognitive, emotional, motor and even neural functioning of the infant (Tronick & Reck, 2009; also see Diego, Jones, & Field, 2010; Diego et al., 2004; Diego et al., 2006; Feldman et al., 2009;

Field, Diego, & Hernandez-Reif, 2009; Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2002; Field et al., 2007) and is associated with increased risk of developing psychopathology in adolescence or young adulthood (Brand & Brennan, 2009; Cicchetti, Rogosch, & Toth, 1998; Gump et al., 2009; Halligan, Murray, Martins, & Cooper, 2007).

III. Maternal behavior is affected by early experiences in family of origin

Overview

As we have seen, how mothers feel at the time they are mothers, whether depressed, anxious or stressed, has an impact on the quality and intensity of their maternal responsiveness. These affective characteristics that exert a proximal influence on mothering behavior have their own origins, often within the mothers' early experiences. In fact, among the most powerful influences on how mothers' mother their infants come from their own experiences growing up. Important aspects of mothering in the child's early life include the quality of the interaction, the warmth expressed by the mother, whether the mother-infant interaction involves predominantly physical contact and play, vocal exchanges, and/or visual mutuality. Also important for mothering is the extent to which mothers respond contingently to their infants, regardless of modality (Bornstein, Tamis-LeMonda, Hahn, & Haynes, 2008; Tamis-LeMonda, Bornstein, & Baumwell, 2001). Contingent responding encompasses the concept of mutuality and is one aspect of mothering that 'empowers' the developing infant by providing an experience of efficacy (for an example see Tamis-LeMonda & Bornstein, 1989). Hence, parents provide experiences through expression of acceptance, affection, liking and caring.

Parents also provide 'negative' and adverse experiences that impact infants and the way they come to parent their own infants when they grow up. Adverse early experiences or early adversity has been operationalized or quantified in a number of different ways, including socioeconomic factors related to housing and parental employment, illness affecting the child or close family members, family discord including parental separation and divorce, and finally, parenting practices and parenting styles (Bifulco et al., 2006; Carpenter et al., 2004; Karevold, Røysamb, Ystrom, & Mathiesen, 2009; Klein et al., 2009; Levitan, Rector, Sheldon, & Goering, 2003; Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996; Rao, Hammen, Ortiz, Chen, & Poland, 2008; Repetti, Taylor, & Seeman, 2002; Rikhye et al., 2008). Here we will focus on early experience and early adversity as they relate to parenting practices and styles. These include physical, sexual and emotional abuse, parental neglect in terms of disinterest in material care and health, direct and indirect

control exerted over the child by the parent, and parental psychopathology such as depression and anxiety. Other known influences on mothers' ability to mother include the stability of their early family environment, the presence of both their primary caregivers as well as other immediate family members (e.g., siblings). In general, these early experiences that mothers have been exposed to affect the subsequent attachment status of the mother-child dyad, reflected in specific maternal behaviors and mothering styles.

Early experiences and intergenerational transfer of mothering styles

There is a growing literature both in humans and in other animals that shows that the quality of mothering received from one's own mother influences the quality of mothering the daughter expresses with her own offspring. For example, in rats, maternal traits such as licking and grooming have been shown to be transmitted across generations (reviewed in Champagne, Francis, Mar, & Meaney, 2003; Fleming et al., 2002; Numan, Fleming, & Levy, 2006). In human mothers, evidence exists for the intergenerational transmission of affective traits (Miller, Warner, Wickramaratne, & Weissman, 1999), parenting styles (Putallaz, Costanzo, Grimes, & Sherman, 1998; Serbin & Karp, 2004; van IJzendoorn, 1992), as well as maternal factors such as bonding and attachment (Benoit & Parker, 1994; Miller, Kramer, Warner, Wickramaratne, & Weissman, 1997; van IJzendoorn, 1992).

How parenting is transmitted across generations and the importance of early experience in the family of origin are just really beginning to be understood, mostly at the cognitive or behavioral level in human moms. There is, however, a large body of work on the behavioral and biological bases of the intergenerational transmission of maternal style in rat mothers and as this work is relevant to the present discussion we will now describe it in brief. Four major components of maternal behavior in rats are retrieval behavior, nest building, nursing behavior, and pup grooming, which includes licking (Numan & Insel, 2003). In rat studies of mothering, the best approximation of variation in maternal care is demonstrated by the elegant studies of Michael Meaney and his students in which they show that the licking exhibited by mother rats shows a very large variation, variation that influences the quality and intensity of the licking behavior of their female offspring that become the next generation of mothers (Champagne & Meaney, 2001). The observation from cross-fostering studies that the licking profile of offspring is determined by their preweaning experiences (hence, the pattern shown by the foster mothers) and not by their genetic origins suggests that the postnatal experiences of the young are crucial to their later behavior with their own off-

spring (Champagne & Meaney, 2001). Thus, as we would expect, maternal behavior deficits observed in adulthood are related to the degree of maternal deprivation received as a neonate (Gonzalez, Lovic, Ward, Wainwright, & Fleming, 2001; Lovic et al., 2001; Rees, Akbari, Steiner, & Fleming, 2008) and, importantly, observed behavioral differences are accompanied by structural brain changes (Burton et al., 2007; Chatterjee et al., 2007; Gonzalez & Fleming, 2002). Offspring of high licking moms become high licking moms (Champagne & Meaney, 2001). Rat pups reared in isolation from their mother and without such stimulation, however, show maternal behavior deficits in behaviors such as crouching and licking (Gonzalez et al., 2001; Melo et al., 2006), an effect that is retained even towards foster pups (Palombo, Nowoslawski, & Fleming, 2010). Furthermore, deficits are related to the degree of early maternal separation with more extreme separation paradigms associated with the most severe behavioral deficits (Lovic et al., 2001; Rees et al., 2008). Maternal separation and the associated reductions of stimulation in pups are further related to the progressive dysregulation of physiological processes in the offspring as well as behavioral deficits related to social learning, sustained attention, inhibition of acoustic startle, and perseveration. It is generally accepted that early experience, notably the quality and quantity of maternal care, influences the plasticity and function of set of brain structures that are genetically mandated to express maternal behavior; this circuit interfaces with brain structures that mediate emotion, sensation, perception, memory and cognitive functions.

In human mothers, research also suggests that early adversity as indexed by quality of care in the family of origin may also affect subsequent parenting (Belsky, 1984; Champagne & Meaney, 2001; Fleming et al., 2002; Maestripieri, 2005). The significance of this statement is underscored by the fact that maternal history of abuse has been proposed as a risk factor for child maltreatment. Approximately 30% of mothers who were abused as children go on to abuse their own children, compared to 5% in mothers not reporting abuse (Knutson, 1995). While the mechanisms underlying a posited 'cycle of abuse' are not well understood, as previously noted, there is support for the intergenerational transmission of parenting styles, which includes factors such as bonding, attachment and maternal rejection (Benoit & Parker, 1994; Miller et al., 1997; Serbin & Karp, 2004; van IJzendoorn, 1992). Moehler, Biringen, and Poustka (2007) analyzed whether emotional availability measured during mother-infant interaction is altered by experiences of physical or sexual abuse in the mother's family of origin. Results revealed that mothers with a history of physical or sexual abuse were significantly more intrusive toward their children than were control mothers. The relationship between maternal early experiences and perceived

parental stress has also been examined. In a study of 120 mothers, Willinger and co-authors (Willinger, Diendorfer-Radner, Willnauer, Jörgl, & Hager, 2005) measured recalled parental bonding and parenting stress and found that higher levels of parenting stress were experienced by mothers reporting less optimal parental bonding. Adverse early experiences are also risk factors for difficulties in mothering, albeit indirectly, through their relationship with maternal psychopathology.

Epidemiological studies indicate that children exposed to early adverse experiences, including those related to bonding and attachment, are at increased risk for the development of depression, anxiety and other stress-related disorders in adulthood (Enns, Cox, & Clara, 2002; Putnam, 2003) and during adolescence (Herrenkohl et al., 2010; Martin, Bergen, Roeger, & Allison, 2004; Rey, 1995). Spertus, Yehuda, Wong, Halligan, and Seremetis (2003) found that a history of emotional abuse and neglect was associated with increased anxiety, depression, posttraumatic stress and physical symptoms and that long-standing behavioral consequences may arise as a result of childhood emotional abuse and neglect, specifically, poorer emotional and physical functioning, factors that would certainly put these women at risk for difficulties in mothering. In addition, an intergenerational effect may account for cyclical occurrence of teenage motherhood (de Paúl & Domenech, 2000; Rebollo & Montero, 2000; Giardino, Gonzalez, Steiner, & Fleming, 2008), where teen mothers often raise poorly adjusted children who tend to become teen parents (Furstenberg, Brooks-Gunn, & Morgan, 1987).

Now a disclaimer! Despite these clear relations between early adversity (and/or retrospective perception of that adversity) and later emotional and parenting problems, the statistic in humans relating to the intergenerational transmission of abuse indicates that 70% of mothers who were abused will NOT abuse their own offspring, indicating that there exists a host of factors that protect prospective mothers from the riskiness of their early experiences. Included among the buffers that are in play are having social supports or a supportive adult somewhere in the environment of the developing child (Jaffee, Caspi, Moffitt, Polo-Tomás, & Taylor, 2007; Kaufman et al., 2004; Wind & Silvern, 1994) as well as forming a partner relationship with a supportive spouse in adulthood (Seeman, Singer, Ryff, Dienberg Love, & Levy-Storrs, 2002). These buffers also speak to the issue of the plasticity of the mothering system. Early experiences can have profound influences on the development of all the constituents that must develop for appropriate mothering to be expressed in terms of affect, attention, learning and so on. And it may well be that the early periods are more susceptible to 'negative' experiences than are the later periods in development (Heim & Nemeroff, 1999; McEwen, 2003); however, experiences acquired later on are either able to reverse earlier

effects or cause development to follow a different path (McEwen, 2003). In support for this, recent work by Bergman, Sarkar, Glover, and O'Connor (in press) demonstrated that the (potentially) deleterious influence of maternal prenatal cortisol on infant development is mediated by mother–infant attachment in the second year of life, with more securely attached toddlers showing no effect of prenatal maternal cortisol on cognitive abilities and insecurely attached toddlers showing a significant, positive relationship.

IV. What has informed us up until this point: Hormones

Basic mechanisms

Hormones play a fundamental role in maternal behavior and have been a focus of much research in animal mothers and only more recently, in humans. Research in rats and other mammals has shown that the hormonal cocktail of pregnancy and parturition, which includes high levels of the peptide hormones, oxytocin and prolactin, against a background of changing levels of steroid hormones, estradiol and progesterone, is essential for the onset and maintenance of maternal behavior (Bridges, 1990; Bridges, 2008; Insel, 1990; Numan et al., 2006; Pryce, Martin, & Skuse, 1995; Rosenblatt, Olufowobi, & Siegel, 1998).

Although evidence for this is stronger in rat compared with human mothers, this hormonal profile is thought to increase mothers' attraction to infant cues, enhance the reinforcing value of pups, and influence affective state (Fleming, Ruble, Krieger, & Wong, 1997a; Numan et al., 2006; Numan & Insel, 2003). In pregnant women, feelings of attachment to the fetus appear to be unrelated to changing levels of pregnancy hormones. However, Fleming et al. (1997a) did find a relationship between hormones and attachment: high attachment to new babies postpartum was related to an increase from early to late pregnancy in estradiol/progesterone ratio and low attachment was related to a decrease in the estradiol/progesterone ratio.

Furthermore, mothers with a greater shift in the estradiol to progesterone ratio across pregnancy also experienced greater feelings of well-being in the postpartum period. Hormones and well-being together explained 40% to 50% of the variance in mothers' attachment (Fleming et al., 1997a). A role for oxytocin in humans is also suggested by recent work by Feldman, Weller, Zagoory-Sharon, and Levine (2007) in which they found that oxytocin levels both during early pregnancy and postpartum were associated with behaviors in mothers normally measured in mother–infant interactions, including gaze, vocalizations, positive affect, and affectionate touch; they also found oxytocin levels related to attachment-related thoughts. These results are

striking in their similarity to what has been described in other mammals and likely reflect an effect of oxytocin in a mother who has been previously primed by estrogen.

Similar to what has been shown in rat mothers (Rees, Panesar, Steiner, & Fleming, 2004, 2006), postpartum hormones from the hypothalamic-pituitary-adrenal (HPA) axis may also be important in mothers' response to their newborns. The HPA axis and HPA-reactivity have been widely studied in humans and animals in the context of emotion, stress and psychopathology (see Heim & Nemeroff, 1999; Heim, Plotsky, & Nemeroff, 2004; McEwen, 2003). We have (Fleming, Steiner, & Anderson, 1987; Corter & Fleming, 1990) examined cortisol in relation to maternal behavior in the early postpartum period when cortisol levels are relatively high and mothers' emotional status is labile. Higher cortisol levels on days 3 and 4 postpartum were significantly and strongly associated with maternal approach behaviors, positive maternal attitudes, or more vocally active infants. Generally, our work suggests that in the early postpartum period (i.e., first postpartum week) in first-time mothers, the HPA system may influence maternal responsiveness by enhancing the salience of infant stimuli and attention to it. Later in the postpartum period (i.e., five to six months postpartum) or in mothers who are stressed and/or 'at risk', however, the HPA axis may have a negative relation with mothering (Krupan, Coombs, Zinga, Steiner, & Fleming, 2005). In short, the precise relation between the HPA system and mothering is unclear and likely varies as a function of the age of the mother, the postpartum period being assessed, the source of the HPA activity (whether through stress or not) and the early experiences of the mother (Gonzalez et al., 2009; Krpan et al., 2005; Stallings, Fleming, Corter, Worthman, & Steiner, 2001).

Depression and HPA function

Activity in the HPA axis has been linked to postpartum depression, albeit inconsistently. Increased cortisol plasma levels have been associated with postpartum depression in some studies (Nierop, Bratsikas, Zimmermann, & Ehlert, 2006), but not in others (Groër & Morgan, 2007; Jolley, Elmore, Barnard, & Carr, 2007; Kammerer, Taylor, & Glover, 2006) and have even been associated with positive affect (e.g., Groër, 2005). As with studies of non-depressed mothers, work suggests that when examining the relationship between cortisol, maternal behavior and mood, factors such as the context for cortisol elevation (e.g., relationship between early life stress and cortisol), maternal age and postpartum stage must be considered. More clues as to the relationship between postpartum depression, cortisol and early experience may be found in the literature on HPA function and non-postpartum depression. Abnormal HPA-axis function has been

frequently observed in major depression. Depression is thought to be characterized by reduced sensitivity of stress-hormone-related negative feedback mechanisms which are associated with larger hormonal response to stressors, higher baseline levels of stress hormones and reduced suppression of the HPA axis in response to the dexamethasone test (Heim et al., 2004). Studies of corticotrophin releasing factor measured in human lumbar cerebrospinal fluid (CSF) have shown increased levels of this stress-related peptide in depressed patients compared to control participants (Banki, Bissette, Arato, O'Connor, & Nemeroff, 1987; Banki, Karmacs, Bissette, & Nemeroff, 1992; France et al., 1988; Nemeroff et al., 1984). When examined post-mortem, the brains of depressed patients have been found to have increased CRF mRNA and increased CRF concentrations in the hypothalamus. In addition, CRF levels in CSF have been found to normalize following successful antidepressant treatment (Nemeroff, Bissette, Akil, & Fink, 1991; Rudorfer, Risby, Osman, Gold, & Potter, 1991). It is important to note that, as with postpartum depression, results for HPA axis function in depression have been mixed; one intriguing explanation given for the disparate results is the notion that HPA function in depression may differ depending on depression subtype (e.g., melancholic, atypical) or on the history of early adversity (Gunnar & Fisher, 2006; Heim et al., 2004).

Early adversity and HPA function

There is little question that adverse early experiences (or early adversity) can lead to heightened stress reactivity that in many cases persists into adulthood. Evidence from animal work suggests that early life experiences related to maternal separation and quality of early maternal care modulate the development of a number of endocrine systems, including the stress system or HPA axis (Champagne & Meaney, 2001). Rat moms who were raised without their mothers or who were raised by mothers who expressed low levels of maternal licking show elevations in postpartum glucocorticoids (Burton et al., 2007; Francis, Diorio, Liu, & Meaney, 1999). Moreover, maternal separation is associated with increased CRF mRNA expression and sensitization of neurons in hypothalamic and limbic regions, decreased glucocorticoid receptor density in the hippocampus and prefrontal cortex, decreased neurogenesis in the hippocampus, as well as altered function of important neurotransmitters (reviewed in Heim et al., 2004). Work on early adversity in primates, where maternal separation or stress paradigms more closely resemble what happens between human moms and infants, has been a bit more complex, demonstrating both HPA axis hypoactivity (Coplan et al., 1996; Rosenblum et al., 2002) and hyperactivity (Fahlke et al., 2000; Higley, Suomi, & Linnoila, 1991, 1992). Results with human children

and adults map onto some animal HPA axis findings quite nicely. Attachment status has been found to influence the reactivity of cortisol secretion in infants (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Nachmias et al., 1996) and adverse early experience has been shown to relate to adrenal response to stress in adolescence (Rao et al., 2008). In adults, in a series of recent studies we found that mothers who were either at-risk teens (Krpan et al., 2005) or clinically depressed (Gonzalez, Steiner, & Fleming, in preparation) were more likely to show less affectionate and disrupted interactions with their infants and had elevated basal cortisol levels. Teen mothers with this endocrine and behavioral profile were also more likely to experience inconsistent care and to have experienced multiple and changing caregivers (Krpan et al., 2005). In addition, adult mothers who were exposed to early adversity (inconsistent care and/or maltreatment) had higher levels of diurnal cortisol (measured from an area under the curve over two consecutive days) and were less sensitive when interacting with their infants (Gonzalez, Steiner, & Fleming, in preparation). The question remains as to whether the elevated cortisol levels in high-risk mothers are especially related to the postpartum period or also present through childhood and adulthood. In fact, a number of retrospective studies have found that outside of the postpartum period, women abused as children do show elevated peak adrenocorticotrophic hormone (ACTH) responses to stress and more prolonged cortisol responses. This effect seems to be strongly related to the woman's current mood state, however, where abused women *without* current depression actually demonstrate decreased cortisol responsiveness and basal cortisol levels and abused women with depression demonstrate features more consistent with hyperactive HPA function (Heim et al., 2004).

Relation of early adversity to depression

It is difficult to talk about hormones, early adversity and depression without integrating the three. In fact, it is also challenging to find research papers where these topics are not interrelated in some manner. Many of the neurobiological effects of early adversity resemble those of depression and, not surprisingly, early adversity is thought to precipitate depression or contribute to a vulnerability to become depressed. One of the strongest risk factors for the development of depression in adulthood is a history of childhood adversity, including parenting factors such as abuse, insecure attachment, parental rejection and lack of warmth (reviewed in Heim, Plotsky, & Nemeroff, 2004; Karevold et al., 2009; Penza, Heim, & Nemeroff, 2003). In terms of depression, early adversity is associated with earlier onset, greater number of episodes, more chronic course of the illness and greater suicidality (Bernet & Stein, 1999; Bifulco, Moran, Baines, Bunn, & Stanford, 2002;

Brown & Moran, 1994; Brown, Cohen, Johnson, & Smailes, 1999; Harkness & Monroe, 2002; Lizardi et al., 1995; McCauley et al., 1997; Moskvina et al., 2007). Some factors thought to mediate the relationship between early adversity and depression are gender (women are more vulnerable), the timing of the early adversity (earlier childhood is a more vulnerable period), the experience of stress in later life and genes (Heim & Nemeroff, 1999; Heim et al., 2004).

Generally speaking, the effects of early adversity on physical and emotional health beginning in early childhood and continuing throughout development are believed to be related to plasticity of the central nervous system as a function of environment and experience. As already noted, stress or trauma experienced during development can permanently shape brain regions that mediate stress and emotion, including the prefrontal cortex and amygdala (Heim & Nemeroff, 1999; Roceri et al., 2004). At the pre-clinical level, much work in animals has also demonstrated that the repeated stress and associated physiology can lead to coordinated changes in numerous behavioral, autonomic and endocrine systems that share features with those observed in depression (for reviews see Heim & Nemeroff, 1999; Kaufman, Plotsky, Nemeroff, & Charney, 2000; McEwen, 2003). A prevailing theory about pathways from early adversity to depression involve the notion that repeated or severe stress early in life is associated with sustained cortisol responses, which is related to brain damage in stress/emotion circuits, which is related to further impairments in stress and emotion responses (Heim et al., 2004). Interestingly, it has also been proposed that not all depression is related to early adversity and that early-adversity precipitated depression may represent a distinct depression subtype (Heim et al., 2004). This suggestion may underscore the importance of examining early experiences in order to understand the nature and etiology of postpartum mood changes.

V. Functional neuroimaging of mothering

Identifying regions of interest

To this point we have described a complex set of psychological and endocrine factors that are known to affect maternal motivation, attitudes, and behavior. What we have not discussed and what follows is an analysis of the growing literature on the neuroanatomy of mothering, taken from both the animal literature and the recent functional magnetic resonance imaging (fMRI) literature. The approach we adopt to understanding that neuroanatomy is to consider functional neuroanatomy that underlies mothering itself as well as the psychological systems that affect mothering and that are discussed above. Included among these are systems related to maternal affect and depression, reward, cognition,

and early experience. How these functional and neural systems interface with the maternal circuitry is what we now explore.

The increasingly widespread use of magnetic resonance imaging (MRI) as a tool to non-invasively investigate the structure and function of the human brain has opened up the field of human neuroscience to a broad number of topics, including maternal behavior. Despite this, there are currently fewer than 20 published investigations of the neuroanatomy of mothering and very few reports of at-risk mom populations. While recent fMRI work (to be detailed later) has made a promising start, there is clearly much work to be done. Despite the relative paucity of human mother studies, when looking to understand the maternal brain in human mothers and when formulating our hypotheses/expectations, we are fortunate to be informed by a large body of work on the maternal brain in animal species.

Animal studies. The neuroanatomy of animal maternal behavior is based predominantly on work with rats, voles, sheep, and primates (summarized in Numan et al., 2006). Taken together, these cross-species studies indicate a striking similarity in the neuroanatomy that underlies mothering. Numan has provided us with an exquisite description and analysis of the functional neuroanatomy of maternal behavior in the rat (see Numan & Insel, 2003; Numan et al., 2006; Numan, 2007). The circuit involves both

excitatory and inhibitory systems. However, most work in the area has focused on the final common path for the expression of the behavior, the medial preoptic area of the hypothalamus (MPOA), and its downstream projections into the midbrain (ventral tegmental area, VTA), hindbrain (periaqueductal gray; PAG) and sensory, limbic, and cortical systems that project into the hypothalamus (see Figure 1). The MPOA region of the hypothalamus contains receptors for all the hormones involved in the activation of maternal behavior, including receptors for estradiol, progesterone, prolactin, oxytocin, vasopressin, and opioids (see Numan et al., 2006). Neurons projecting into the MPOA region of the hypothalamus are also involved in other behavioral changes, including changes in mothers' affect (amygdala, prefrontal cortex), stimulus salience (amygdala and striatum/nucleus accumbens), attention (nucleus accumbens and medial prefrontal cortex), and memory (nucleus accumbens, medial prefrontal cortex). Some of these sites also contain hormone receptors (amygdala, medial prefrontal cortex) and may be the sites where the periparturitional hormones likely act to change behavior at the time of parturition (Numan et al., 2006).

While the rat/animal models of maternal behavior are elegant and informative and have identified some key regions in a putative mothering circuit (e.g., hypothalamus, amygdala, prefrontal cortex, nucleus accumbens), we know that the brains and behaviors

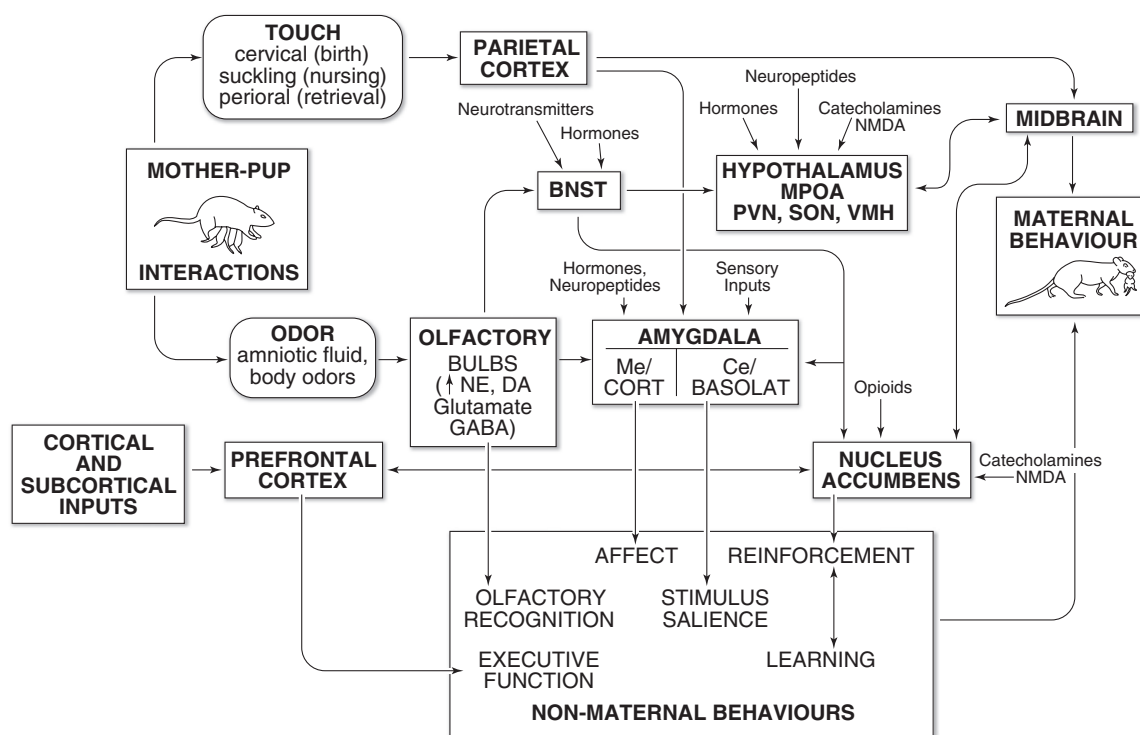


Figure 1 Functional neuroanatomy mediating maternal and related behaviors in mammals. Neuroanatomical structures include olfactory bulbs, amygdala, nucleus accumbens, bed nucleus of the stria terminalis (BNST), medial preoptic area (MPOA), ventromedial hypothalamus (VMH), periventricular nucleus (PVN), supraoptic nucleus (SON), midbrain, and parietal cortex. Relevant neurochemistry includes the catecholamines norepinephrine (NE), and dopamine (DA), the neuropeptides, and the opioids

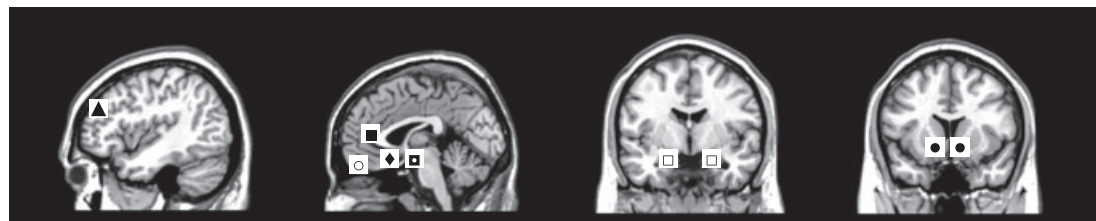
of human mothers and mother–infant interactions are far more complex than in lower mammals. Thus, while animal work provides one important framework, we must consider other brain systems as well. As already noted, to mother appropriately requires the action of multiple behavioral systems in the domains of sensation, perception, emotion and motivation, reward, executive function, motor output and learning. As a mother–infant dyad are interacting, the mother is receiving sensory input about how her child looks, sounds and smells, she has feelings that may change rapidly in the moment and also a baseline level of affect that may not be situation dependent, she is moving, touching, kissing, speaking, singing, rocking, reacting, she is attending and sometimes spreading her attention across a number of activities or stimuli, she is thinking about her child and perhaps other things and sometimes planning and controlling the nature of play. She is busy. Of course, as for essentially all experimentally manipulated or scientifically observable human behavior, every region of the brain and all major brain systems are active, in some manner. The brain does not have an off switch.

One strategy to reduce this complexity adopted by us (and others), however, is to focus on neural systems that are particularly relevant or compelling in the context of mothering: (a) social behavior; (b) reward and affect; (c) executive function; and, of course, (d) maternal behavior. Studies examining maternal behavior will be discussed last, not as a reflection of their (in)significance but rather to emphasize the broad overlap between work investigating maternal behavior proper and work investigating strongly related psychological constructs. After we have examined systems we feel contribute to and interact with systems mediating maternal behavior, we can more thoughtfully discuss imaging studies looking at maternal response to infant stimuli in the context of regions of interest (see Figure 2): Hypothalamus/MPOA (maternal behavior, drive states), nucleus accumbens (stimulus salience, affective valence), amygdala (emotion/affect response and regulation, affective valence), anterior cingulate cortex (affect response and regulation, affective valence, stimulus salience, executive function, social cognition), orbitofrontal cortex (stimulus salience, affective valence, executive function), dorsolateral prefrontal cortex (affect regulation, executive function). To aid the reader in this anatomical journey we include a schematic of the neural regions that will be discussed as well as a table listing the different neural structures, their known functions, and the relevant references (see Figures 2 and 3).

Social behavior, reward and affect

Social behavior. As mother–infant interaction is, broadly speaking, a social behavior, a focus on mothering within the context of social behavior is

appropriate. The study of social behavior and related constructs (e.g., social cognition, affiliation, love, attachment/bonding, empathy) is concerned with our perceptions of and interactions with familiar and unfamiliar others. The related fMRI studies have used a number of different paradigms using social stimuli, including reading empathy-eliciting scripts, exposure to stimuli of loved ones and exposure to emotional social stimuli (e.g., faces) with and without contextual factors. Brain regions that are commonly identified in these studies include the amygdala, anterior cingulate cortex (ACC) and dorsal and ventral striatum (e.g., Kim et al., 2009a; Kirsch et al., 2005; Platek & Kemp, 2009; Zahn, de Oliveira-Souza, Bramati, Garrido, & Moll, 2009); these brain regions are more generally implicated in emotion perception/regulation, action initiation and stimulus valence/salience and are also known to contain receptors for hormones thought to be important in social behavior (i.e., oxytocin, vasopressin; Debiec, 2005; Huber, Veinante, & Stoop, 2005; Keverne & Curley, 2004; Schorscher-Petcu, Dupré, & Tribollet, 2009; Smeltzer, Curtis, Aragona, & Wang, 2006). Studies of social cognition typically involve response to emotional and non-emotional human faces (e.g., Kirsch et al., 2005; Mitchell, Neil Macrae, & Banaji, 2005; Schulz et al., 2009). Kirsch and colleagues (2005) added the administration of the ‘affiliative’ peptide, oxytocin, to a social cognition paradigm which involved responding to an emotional (angry, afraid) face-matching task. Intriguingly, the authors found that the administration of oxytocin attenuated the expected amygdala response to the negative social stimuli (faces). Amygdala response to emotional or other self-referential faces is complex with increased activity in the amygdala associated with negative faces (e.g., fearful faces; Gamer & Büchel, 2009), positive faces (Derntl et al., 2009; Killgore & Yurgelun-Todd, 2004; Williams, McGlone, Abbott, & Mattingley, 2005) and familiar faces (Platek & Kemp, 2009). In contrast, some studies also report a decrease in amygdala activity in response to familiar faces (e.g., Bartels & Zeki, 2004). These discrepant findings could reflect the multifaceted role of the amygdala in the processing of emotional and/or social stimuli: the amygdala is involved in basic stimulus perception, the integration of stimuli with an affective ‘value’ and organizing output to guide affective, autonomic and behavioral responses (reviewed in Gobbini & Haxby, 2007). The amygdala’s function in integrating multiple brain systems in order to guide behavior is also sensitive to contextual demands (e.g., task requirements, environment), stimulus valence as well as, perhaps, the mood and affect of the individual. Thus, as with animal models, a positive relationship between activity in the amygdala and positive mothering behavior cannot be assumed and numerous factors should be considered when evaluating the role of the amygdala in maternal behavior.



Brain Region	Location and Function
▲ Dorsolateral prefrontal cortex	<ul style="list-style-type: none"> •Lateral surface of the frontal lobes, corresponds to Brodmann areas 9, 46 and 9/46 (Petrides & Pandya, 1999) •Top-down control of cognitive and emotional processes, executive function, mood and emotion regulation (Davidson, 2002; Petrides, 2005; Koenigs & Grafman, 2009)
○ Orbitofrontal cortex	<ul style="list-style-type: none"> •Orbital surface of the frontal lobes, corresponds to Brodmann areas 10, 11 and 47 (Kringelbach, 2005) •Reward, impulsivity and response inhibition, affect/emotion, visceral function (Kringelbach, 2005; Milad & Rauch, 2007; Critchley, 2009; Shoenbaum et al., 2009)
■ Perigenual anterior cingulate cortex	<ul style="list-style-type: none"> •Medial surface of the frontal lobes, corresponds to Brodmann areas 24 and 32 around the genu of the corpus callosum (Carmichael and Price 1994; Vogt et al. 1995, 2005) •Affect/mood regulation, integrating information from the internal milieu to aid in response generation or behavioral control, social cognition (Paus, 2001; Lam, Batson & Decety, 2007; Drevets & Savitz, 2008; Chaudry et al., 2009; Wang et al., 2009)
◆ Subgenual anterior cingulate cortex	<ul style="list-style-type: none"> •Medial surface of the frontal lobes, corresponds to Brodmann area 25, 24 and 32, located below the genu of the corpus callosum (Carmichael and Price 1994; Vogt et al. 1995, 2005) •Affect/mood regulation, integrating information from the internal milieu to aid in response generation or behavioral control, anxiety and depression and associated functions (e.g., arousal, stress response) (Paus, 2001; Bremner et al., 2008; Johansen-Berg et al., 2008; Drevets & Savitz, 2008)
□ Hypothalamus	<ul style="list-style-type: none"> •Ventral portion of the diencephalon •Motivated behavior, homeostatic and neuroendocrine functions, including blood pressure, heart rate, hunger, thirst, sleep, sexual and maternal behavior, also emotion (Risold et al., 1997; Sowards & Sowards, 2002, 2003)
□ Amygdala	<ul style="list-style-type: none"> •Medial temporal lobes, at the head of the hippocampus •Stimulus perception, integration of stimuli with an affective value and organising output to guide affective, autonomic and behavioural responses, also mood/anxiety and stress (Shin, Rauch & Pitman, 2006; Gobbini & Haxby, 2007; Sergerie, Chochol & Armony, 2008; Drevets, Price & Furey, 2008; Dedovic et al., 2009)
● Nucleus Accumbens	<ul style="list-style-type: none"> •Part of the ventral striatum •Dopamine, integrates information from subcortical regions and prefrontal cortex, involved in motivated behaviors, especially those related to emotion and reward, also addiction and depression (Ikemoto & Panskeep, 1999; Di Chiara, 2002; Goto & Grace, 2005, 2008; Giacobbe, Mayberg & Lozano, 2009)

Figure 2 Brain structures thought to be important in human maternal behaviour. Note that these structures are comprised of classic maternal regions such as the hypothalamus, as well as regions with primary functions important to maternal behaviour. The top panel illustrates the approximate anatomical location of each region; the bottom table contains a coded legend describing each region in terms of location and function

Investigating more abstract concepts related to social behavior, a recent study by Kim and colleagues (2009a) examined the neural correlates related to compassionate concerns which was defined as 'related to the motivation to approach, help, comfort or otherwise alleviate suffering' (Kim et al., 2009a). During fMRI, male and female participants completed a task that involved a passive

condition of simply viewing a set of sad faces and an active condition where participants were instructed to view the face while attempting to feel/share/understand the person's suffering. Viewing neutral and sad faces with a 'compassionate attitude', compared with passive viewing, was related to increased activity in the medial prefrontal cortex (including subgenual ACC), dorsal and ventral striatum as well

as the insula, thalamus and periaqueductal grey. The authors interpreted their results in the context of Theory of Mind, which has been associated, among other areas, with activity in the medial prefrontal cortex (Saxe, Moran, Scholz, & Gabrieli, 2006; Schulte-Rüther, Markowitsch, Fink, & Piefke, 2007; Spreng & Grady, 2009). As previously noted, Theory of Mind, a theory about how we understand the intentions and emotions of others, has obvious implications for individual differences in mothering, where correctly identifying and responding to infant signals is key. One aspect of Theory of Mind reasoning is that we understand the internal states of others (and hence experience empathy) by simulating their experience at the neural level (Blakemore & Decety, 2001; Rizzolatti & Fabbri-Destro, 2008; Schulte-Rüther et al., 2007). An extension of this notion is that our ability to understand the mental world of another is tied to mirror neuron activity, that is, brain response that is related to observation of another that mimics the brain response associated with the (other) occurring thought/emotion. This idea was first described as a motor phenomenon (see the excellent work of G. Rizzolatti; for a review see Rizzolatti & Craighero, 2004), but it has recently been applied to social cognition (e.g., Rizzolatti & Fabbri-Destro, 2008; Schulte-Rüther et al., 2007). Recent work has also linked Theory of Mind to the Default Mode Network, a core set of brain regions involved in reflecting on the past, present and future and on the minds of others that also includes the medial prefrontal cortex as a main player (Spreng & Grady, 2009).

Relatedly, Zahn and colleagues (2009) were also interested in the role of the subgenual ACC in empathic concern and noted that this region may be particularly important when stimuli are self-relevant and/or reflect individual differences in empathic behavioral response. In this study, a behavioral index of empathic concern was obtained from male and female participants and was later correlated with subgenual ACC response to reading scripts designed to elicit feelings of guilt compared with a control condition. The authors reported that subgenual ACC activity while reading the guilt-eliciting scripts was positively associated with an individual's level of empathic concern, with higher levels of empathic concern related to greater activity in the subgenual ACC. The ACC is an especially interesting region as its patterns of connections make it an ideal structure to integrate information about the internal milieu to guide action, subjective feeling or thought. The subgenual ACC in particular, with its strong connections with the amygdala and nucleus accumbens, is also believed to play a more general role in affect regulation and motivation.

Finally, much research in the area of social behavior has sought to investigate the neural correlates that underlie feelings of love for romantic

partners as well as for offspring. In an influential study, Bartels and Zeki (2000) found that viewing pictures of romantic partners compared with friends was related to increases in activity in the striatum, ACC, periaqueductal grey, insula and hippocampus and, interestingly, decreases in activity in regions of the prefrontal cortex (Bartels & Zeki, 2000). It is of note that this pattern of activity was also observed, in a separate study, for own children compared with familiar children (Bartels & Zeki, 2004). The authors conclude that love relationships are (should be) inherently rewarding and must be to ensure the perpetuation of the species. Thus, human attachment may be associated with increased activity in reward-related brain regions and, perhaps, decreased activity in brain regions involved in negative affect and/or negative social evaluation. Indeed, in humans as in animals, there has been much support for the involvement of dopamine-rich regions of the striatum in feelings of love and attachment (Fisher, Aron, & Brown, 2005; Aron et al., 2005).

Reward and affect. Mothering and nurturance are also often grouped within basic drive states of sexual desire, hunger/thirst, fear, power-dominance, etc. (Sewards & Sewards, 2003). As already mentioned, as infant (and species) survival depends on it, we expect that most mothers will be *motivated* to display maternal care to some extent and given the right circumstances and history, will find themselves more attracted to their babies than repulsed by them. That is, with birth, the balance of approach to avoidance will tip in favor of approach and increasingly so with additional positive experience. In animal models, maternal behavior has been framed in the context of approach-avoidance tendencies, where the onset of maternal behavior occurs when the tendency to avoid pups, find them aversive and/or view them with indifference is suppressed and the tendency to approach pups and find them rewarding and/or pleasant is enhanced (Fleming & Rosenblatt, 1974a, 1974b; Numan, 2007; Rosenblatt, 1969, 1975a). In the animal model, brain systems that initially mediate fear and avoidance include the olfactory bulbs and tracts, the medial amygdala, the bed nucleus of the stria terminalis, and the ventromedial hypothalamus (VMH); prior to late gestation, these systems inhibit the MPOA. However, with hormonal priming during late pregnancy and with parturition, these systems come under inhibition and pup odors which prior to birth were initially avoided take on a positive valence when the pups are born. It is of note that this priming can also occur in virgin females, to some extent, by prolonged experience with or exposure to pups. Thus, the inhibition that the MPOA is under in the virgin animal is removed when gestational/parturitional hormones are present or when a virgin experiences sensitization. One can think of this as disinhibiting the

inhibition that the MPOA is under from the amygdala, through the VMH. This motivational model of mothering involves brain systems important in stimulus salience and valence, for example, how positive pups are and how rewarding they become with experience, or how anxiety-inducing pups are.

There is certainly evidence at the behavioral level for changes in infant-related stimulus salience and emotion in mothering in human moms. Compared to mothers, non-mothers find infant odors less pleasing and show a different autonomic and emotional (i.e., emotion ratings) response to infant cries (Fleming, Steiner, & Corter, 1997b; Giardino et al., 2008; Stallings et al., 2001). In addition, a mother's own feelings of attachment to her baby increase over the course of her pregnancy, a phenomenon that may also reflect an increase in or readiness for 'approach' behaviors. However, as we are talking about motivation, affect and reward, terms which have been used interchangeably in some studies, we must emphasize that, in our conceptualization, mothering represents a motivated behavior that has an impact on and interacts with reward and affect systems.

Not surprisingly, in humans, the findings of neuroimaging studies focusing on reward and affect show considerable overlap with brain regions that are activated in mothers by infant cues; these include the prefrontal cortex (ACC, orbitofrontal cortex (OFC)), striatum (nucleus accumbens), amygdala and hypothalamus. In a striking example of the overlap between mothering neural circuits and those involved in affect (mood), Johansen-Berg and colleagues (2008) examined the connectivity of the ventral ACC, the anatomical target of deep brain stimulation that has alleviated depression in some patients (Mayberg et al., 2005). The anterior cingulate cortex has been widely implicated in the regulation of mood, including major depression, as well as anxiety (Drevets, Savitz, & Trimble, 2008). Using tractography of diffusion imaging data, which allows for the in-vivo mapping of white-matter tracts, the authors confirmed in humans what has been established in animals: the anatomical connections between the ACC and the hypothalamus, nucleus accumbens, amygdala, OFC, dorsomedial frontal cortex and frontal pole (Johansen-Berg et al., 2008). Depression is characterized by impairments in (or *depression of*) other drive states that operate on the same neuroendocrinological systems as maternal behavior (e.g., sexual desire, hunger/thirst, sleep) and is also characterized by impairment in reward processing (e.g., pleasure of interest in people and activities) which is known to be critical in the activation of maternal behavior. Thus, it is not surprisingly that mothering and depression share so much overlap in terms of brain systems, nor is it surprising that depression has such a powerful impact on the capacity for, or motivation to, mother.

Anxiety is also an important affective state that is relevant to animal models of mothering and is also strongly comorbid with depression. In fact, for the most part key cortical and subcortical structures implicated in the stress response (and also, the deleterious influence of early adversity) also completely overlap with those involved in mothering (e.g., the prefrontal cortex and amygdala; see Kaufman et al., 2000). Much research examining stress and fear-related processes, including anticipatory anxiety, have demonstrated a role for the ACC and the amygdala (e.g., Barrett & Armony, 2009; Nitschke et al., 2009; Sarinopoulos et al., 2009). One model of fear/anxiety learning and extinction posits that inhibition of the amygdala by the ACC is important in learning when a fear or stress response is appropriate and when it is not. Some work has also linked deficits in this system to mechanisms underlying the development of maladaptive fear responses as in post-traumatic stress disorder (reviewed in Rauch, Shin, & Phelps, 2006), the pathology of which is thought to share similar mechanisms with early adversity.

Given the motivational model of mothering in the rat, it will be interesting to examine further whether or not there exists an infant-related avoidance tendency in human women and if a similar ACC-inhibition of the amygdala may be related to a shift from avoidance to approach tendencies. An obvious problem with this suggestion is that human women rarely show overt avoidance of infants and in fact the opposite is often true for both nulliparous and multiparous mothers (see Glocker et al., 2009). However, differences do exist in terms of emotional and autonomic response to infants in nulliparous and multiparous mothers and there are often vast differences in the nature of responsivity to infants across mothers. It is also important to note that imaging studies have suggested that human attachment may be associated with increased activity in reward-related brain regions and, perhaps, decreased activity in brain regions involved in negative affect and/or negative social evaluation (Bartels & Zeki, 2004). It is possible, then, that a similar motivational push-pull exists in human mothers, albeit to a more subtle extent. In other words, in a human model the 'push' side of things may not be characterized by the unmistakable hostility or avoidance that has been observed in inexperienced or virgin rats, but by negative affect and anxiety or more subtle signs of rejection (e.g., looking away from the infant, negative comments about the infant). It is also possible that functional differences in important regions in such a push-pull circuit, for example hyperactivity of the amygdala and/or lack of inhibition by the ACC, in response to the infant, may explain variability in quality of mothering behaviors.

In terms of what is known about the neurocircuitry of reward, a great deal of focus has been on the dopamine system and neural structures rich in

dopamine receptors or key structures in dopamine-related brain circuits. Based on animal work, these regions include dopamine centers in the midbrain and the striatum (e.g., nucleus accumbens) and connected cortical regions (medial prefrontal cortex, OFC; Hollerman, Tremblay, & Schultz, 2000; Wise, 2000). There is now a substantial animal literature showing that the nucleus accumbens is important for maternal behavior and that dopamine is released in this site in response to pups or pup cues in new mother rats, experienced mother rats and virgins induced to be maternal through simple exposure (i.e., sensitized virgins) (Afonso, Grella, Chatterjee, & Fleming, 2008; Afonso, King, Chatterjee, & Fleming, 2009; Champagne et al., 2004; Mattson & Morrell, 2005; Olazábal, Abercrombie, Rosenblatt, & Morrell, 2004). Moreover, there is substantial evidence that the dopamine release profile to pups in mothers depends on the action of the parturitional hormones and is different from the profile of dopamine release to food in these mothers (Afonso et al., 2009). It is different as well from the profile shown by sensitized virgins, but not the profile shown by hormonally primed virgins (Afonso et al., 2008, 2009).

Human work has for the most part confirmed the (non-maternal) animal findings in imaging studies examining the rewarding nature of food (Goldstone et al., 2009; Grabenhorst, Rolls, Parris, & d'Souza, 2009), social acceptance (Davey, Allen, Harrison, Dwyer, & Yücel, 2009), money (Fujiwara, Tobler, Taira, Iijima, & Tsutsui, 2009; Simon et al., 2010) and, appropriately, infantile physical features (Glocker et al., 2009). While this recent work has confirmed posited reward structures and circuits, it has also revealed more subtle features and functionality of specific regions in this circuit. For example, Carter, Macinnes, Huettel, and Adcock (2009) examined the degree to which the striatum encodes both the motivational and affective relevance of anticipated outcomes. To do this, men and women completed a reward anticipation task during fMRI where monetary gains and loss outcomes could be either self- or charity-directed. They found that activity in the nucleus accumbens and ventral tegmental area was increased in anticipation of both gain and loss trials, supporting the notion that these regions are sensitive to the motivational relevance (salience), not the valence, of an event. Evidence regarding the specificity of response in the nucleus accumbens to stimulus salience versus valence is unclear, however, as it has also been demonstrated that accumbens activity correlates with *both* gains and losses only in conditions of uncertainty (Cooper & Knutson, 2008). An attempt has been made to reconcile these findings by noting that while the nucleus accumbens may be primarily sensitive to stimulus salience (e.g., reward-based or not reward-based), its response may be influenced by affective valence (e.g., gain or loss), especially in

individuals who are reward sensitive (Carter et al., 2009).

It is of note that an equally complicated formulation has also been proposed for the OFC and reward (see Kringelbach, 2005), which, depending on the subregion, is implicated in response to rewards of varying complexity (e.g., gain/loss versus taste) as well as positively versus negatively valenced reward stimuli. In addition, subregions of the ACC have also been associated with gain-specific (perigenual ACC), and gain- and loss-specific (supragenual ACC) change in activity in a manner consistent to what has been observed for positive and negative emotions (Fujiwara et al., 2009). Generally speaking, such distinctions may be important in studies of maternal response using positive and negative infant faces or in mothers with varying sensitivity to reward and affect stimuli (related to affective state, stress, early experience, etc.). Related to this, recent fMRI work has demonstrated that childhood adversity influences the neural (basal ganglia) and behavioral (emotion rating) response to monetary reward in adults, where individuals exposed to childhood adversity demonstrated attenuated brain response to reward cues in the globus pallidus and rated reward cues less positively (Dillon et al., 2009). This work nicely complements animal studies that have demonstrated a relationship between adverse rearing experiences related to maternal separation and altered responses to both rewarding and aversive stimuli (Nelson et al., 2009; Pryce, Dettling, Spengler, Spaete, & Feldon, 2004).

Not surprising, numerous fMRI studies have also demonstrated depression-related alterations in neural and behavioral response to emotional and/or rewarding stimuli (Dannowski et al., 2007, 2008; Dichter, Felder, & Smoski, 2009; Fu et al., 2008; Gray et al., 2006; Raes, Hermans, & Williams, 2006; Smoski et al., 2009). People with depression exhibit negative biases in processing facial expressions, altered activity in emotion-related brain regions in response to emotion faces (e.g., greater amygdala response to emotional faces) as well as blunted response to positive or rewarding stimuli (Dannowski et al., 2007, 2008; Dichter et al., 2009; Fu et al., 2008; Gray et al., 2006; Raes et al., 2006; Smoski et al., 2009). In a recent study investigating the reward system, Pizzagalli and co-authors (2009) examined activity in the striatum in patients with depression while they completed a monetary reward task. As expected, compared to control participants, participants with depression showed blunted response to monetary gain in the nucleus accumbens. Interestingly, depression severity was also associated with reduced volume in the caudate nucleus.

Executive function

We know that optimal mothering requires that the mother pays attention to her infant, that

she responds appropriately to her infant and that she responds contingently to the infant's cries and behavior. As indicated earlier, she must be flexible and be able to focus when appropriate and switch attention when the situation changes. And finally, she must retain information about the infant and adequately manipulate the environment to optimize it for the infant. In light of these cognitive demands, the activity of brain regions mediating planning, attention, flexibility and working memory are essential for adequate mothering and thus constitute the focus of a number of maternal studies.

Given its role in attention, cognitive flexibility and working memory, the dorsolateral prefrontal cortex (DLPFC) appears an ideal structure to help identify and attend to infant cues in a complex environment, efficiently switch-tasks and attention and maintain/manipulate information for on-line decision-making and action planning. Over the past decade or so, there has been much debate regarding the function of the DLPFC and whether this region is organized in a 'domain-specific' (i.e., visuo-spatial versus verbal) or 'process-specific' (i.e., monitoring versus retrieval) manner. Supporting the latter, the detailed work of Michael Petrides has contributed much to our understanding of the function of the DLPFC (specifically, the mid-dorsolateral prefrontal cortex, corresponding to areas 46 and 9/46), which he sees as:

a system for the conscious active control of planned behavior and cognition. Such a system must have the capacity to hold abstract coded representations of events that are expected to occur, so as to mark their occurrence or non-occurrence (i.e. monitor their relative status in relation to each other and the intended plan). Furthermore, such a system would be involved in the manipulation of these cognitive representations (i.e. planning) since such manipulation would require constant monitoring of the relative status of intended acts or events (Petrides, 2005).

Although executive functions rely on interactions between many brain regions (for reviews see Duncan & Owen, 2000; Leh, Petrides, & Strafella, 2009), numerous neuroimaging studies in humans have highlighted an important role for the DLPFC in tasks that involve task- or set-shifting (e.g., Monchi, Petrides, Petre, Worsley, & Dagher, 2001; Nagahama et al., 2001; Ravizza & Carter, 2008), auditory and spatial attention (Krumbholz, Nobis, Weatheritt, & Fink, 2009), attention related to perceptual selection (Nee & Jonides, 2009), working memory involved in the Iowa Gambling Task (Li, Lu, D'Argembeau, Ng, & Bechara, 2009), solving anagrams with varying degrees of abstraction (Christoff, Keramiatian, Gordon, Smith, & Mädlar, 2009), memorial selection (Nee & Jonides, 2009) and active maintenance of information for ongoing task performance (Cole & Schneider, 2007).

Other regions of the frontal lobes that are relevant to maternal behavior also have prominent roles in executive functions: the ACC and OFC. The dorsal

anterior cingulate cortex has been widely linked to tasks involving attention and action monitoring, especially in the context of error or conflict (Barch, Braver, Sabb, & Noll, 2000; Brown & Braver, 2005, 2008; Modirrousta & Fellows, 2008; van Veen & Carter, 2002; Wang, Ulbert, Schomer, Marinkovic, & Halgren, 2005) and the orbitofrontal cortex has been linked to impulse control (Horn, Dolan, Elliott, Deakin, & Woodruff, 2003; Matsuo et al., 2009; reviewed in Fineberg et al., 2010; Winstanley, Theobald, Cardinal, & Robbins, 2004). While the relationship between prefrontal cortex function and maternal behavior has not been widely investigated, there is considerable evidence that both early adversity and non-postpartum depression have an impact on the structure and/or function of the prefrontal cortex (animal studies: Banasr et al., 2007; Roceri et al., 2004; Roth, Lubin, Funk, & Sweatt, 2009; human studies: Clark, Chamberlain, & Sahakian, 2009; Hercher, Turecki, & Mechawar, 2009; Koenigs & Grafman, 2009; Rogers et al., 2004; Savitz & Drevets, 2009; Siegle, Thompson, Carter, Steinhauer, & Thase, 2007) and in some cases structure and function have been linked. For example, in rats, early experience-mediated deficits in executive function-processes such as prepulse inhibition (PPI) and set-shifting (Burton et al., 2006; Garner et al., 2007; Lovic & Fleming, 2004) are accompanied by structural changes in the pre-frontal cortex (PFC) (Burton et al., 2007; Chatterjee et al., 2007). Further work is needed, however, to confirm the predicted importance of prefrontal function in maternal behavior both outside of and in the context of important individual differences such as early experience and mood.

Maternal behavior

Work on the neural bases of maternal behavior in humans is derived primarily from fewer than 20 fMRI studies where mothers, non-mothers, and sometimes fathers are presented with either pictures of infants (Barrett et al., 2009; Bartels & Zeki, 2004; Leibenluft, Gobbini, Harrison, & Haxby, 2004; Nitschke et al., 2004; Strathearn, Fonagy, Amico, & Montague, 2009; Strathearn, Li, Fonagy, & Montague, 2008), recorded infant cries (Lorberbaum et al., 2002; Seifritz, 2003; Swain et al., 2008), or videotapes of infants (Noriuchi, Kikuchi, & Senoo, 2008; Ranote et al., 2004). For thorough and insightful reviews of the literature see recent papers by James E. Swain and colleagues (e.g., Swain, 2008; Swain, Lorberbaum, Kose, & Strathearn, 2007). By examining these studies (many are reviewed in Swain & Lorberbaum, 2008 and Swain et al., 2007), we can get an idea about the specificity of our posited maternal systems of interest to infant type (own, other), stimulus type (infant vs. non-infant) as well as stimulus familiarity, modality (auditory, visual, both) and even subject (mother, non-mother). For the

most part, the findings of fMRI work on the maternal brain demonstrate that irrespective of stimulus modality (e.g., visual or auditory) or stimulus familiarity (see Leibenluft et al., 2004), many of our maternal regions of interest (e.g., hypothalamus, nucleus accumbens, amygdala, anterior cingulate cortex, orbitofrontal cortex, dorsolateral prefrontal cortex) are implicated in response to a mother's own infant compared to another infant or non-infant control. In studies comparing parents to non-parents, neural response to infants in maternal regions have also been found to be specific to parental status (e.g., Seifritz et al. 2003, but see Glocker et al., 2009 for a demonstration of how infant schema are rewarding for nulliparous women). That is, as we would expect, one's own infant is a special stimulus that engages brain regions that we know are important in maternal behavior and related systems (e.g., executive function, reward, affect). As the role of these systems in maternal behavior has not yet been addressed in a detailed manner, we cannot yet determine the functional significance of identified maternal regions in the context of the many domains involved in mothering. Indeed, the current state of literature on the human maternal brain holds many more questions than answers and we find that there are large differences across studies in what and how 'maternal' regions are implicated. In what follows we briefly discuss a few key areas that could influence brain imaging results. Also, we talk about how identifying and understanding important individual differences may help move this area of research forward.

Although no imaging paradigm will give us a spotlight on a maternal circuit, different patterns of results observed across maternal imaging studies can be attributed to factors such as the age of children studied (newborn to early childhood) and the comparison used to best capture the maternal brain (own baby compared to control stimuli, familiar infant or unfamiliar infant). In regard to the former, the early postpartum period is a unique time, both hormonally and behaviorally; the mother is learning much about her infant at this time, attachment patterns are forming, the maternal system may be especially primed for action and one would predict that this would be a time of great activity for brain systems important in maternal behavior. In fact, a main function of the maternal system in the early postpartum period is ensuring that the mother will respond to her infant, will find her infant pleasing and is attracted to her infant, is attentive, sensitive, etc. There are great differences, of course, across mothers in terms of the quality and quantity of these maternal behaviors and we predict that these differences are related to differences in the function of the maternal system. One may further predict that later on and in the postpartum period and throughout the life of the child, once the nature of mother-child relationship is more habitual and consolidated

and the hormones of parturition are not as influential on the brain and behavior, the function and/or response of maternal neural systems may be quite different. Given this possibility, examining maternal response to children with a broad range of ages may further add to unwanted 'noise' in the observed maternal system.

Discrepant findings across studies may also be attributed to differences in the experimental paradigm, or specifically, in the comparison used to best capture maternal response. Work on the human maternal brain rests on the acceptance of the notion that we are able to elicit a response in the fMRI scanner that is relevant to and reflective of something as complex as mothering. Capturing maternal behavior or maternal responsiveness in an fMRI scanner is a considerable challenge, however, and as previously noted, choice of a particular paradigm has many implications for how we interpret the results and the likelihood that a particular system or structure will be engaged. The choice of approach is at the discretion of the investigators and thus they tend to vary considerably. For example, some studies have used an unfamiliar infant compared to a control stimulus (e.g., computer-generated noise, house) to capture maternal response; most studies use mothers' own children and contrast responses to them with that of unfamiliar or familiar children. These approaches all have different strengths and weaknesses in regard to ecological validity as well as what can be inferred from the imaging results. One may argue that using a standard infant stimulus (not mother's own infant) in order to capture maternal response may not be as effective in engaging the maternal circuit, the function of which we assume is at least in part specialized for or uniquely connected to the mother's own offspring. That being said, we must concede that it is also possible (and likely) that certain regions within a maternal circuit will respond to any infant stimuli, and perhaps even find such stimuli rewarding compared to a non-infant stimulus, especially for a mother in comparison to a non-mother (see Glocker et al., 2009). Another major question in terms of studying the maternal circuit is in regard to the most optimal comparison stimulus for a mother's own infant. That is, to isolate brain activity associated with a maternal response to one's own infant while controlling for confounding factors or factors of no interest (i.e., the 'infantness' of the face, familiarity of the stimulus, emotionality of the stimulus). Strategies that have been used include a non-infant stimulus (e.g., an object, artificially created sound), an unfamiliar baby or a familiar baby. Using an unfamiliar infant as a control stimulus takes care of many confounds, with the exception of familiarity (of own baby) and novelty (of unfamiliar baby) which could bias results in manner that is not necessarily reflective of maternal response (e.g., Leibenluft et al., 2004). Furthermore, when comparing brain response to own and *familiar* infants to

which there are likely varying degrees of emotion and maternal feelings, there is also the risk that differences in brain regions of interest (especially small subcortical regions) will be too subtle to be detected. Thus, the main message we wish to convey is that the 'perfect' paradigm to identify a maternal circuit does not exist and that we have at our disposal a number of options with strengths and weaknesses that will influence the relevance (in terms of regions of interest) of brain imaging findings to something as complex as mothering.

Another factor that may impact the nature of maternal responsivity in brain imaging studies is maternal experience and parity. Patterns of brain response as a function of mothers' parity or maternal experience have not yet been adequately investigated in humans. However, based on the animal work we can make a number of predictions. In the rat work we know that certain brain regions are more active (established through expression of the *c-fos* gene) in experienced than inexperienced animals when presented with pup stimulation. These areas include sensory areas important for mothering in the rat and here the parietal cortex which mediates touch stimulation is implicated. Other areas that show greater activation in multiparous or experienced animals over primiparous animals include the MPOA (the so-called final common pathway) and the anterior cingulate region (Fleming & Korsmit, 1996).

Recent animal work also shows that the parity differences that are seen in brain activation patterns relate more to the presence and absence of mothering experience than to variations in mothers' hormonal profile, although hormones may well enhance or intensify brain responses to pups in maternal animals. For instance, virgin rats who become maternal through sensitization to pup stimulation, through simple exposure, show the same pattern of brain activation as do primiparous mothers who become maternal through hormonal mechanisms. The pattern of effects is the same in the two cases, although the hormonally primed primiparous animal shows a more 'robust' activation pattern than does the sensitized virgin animal when presented with pups, suggesting a role for the hormonal activation of behavior (Numan et al., 2006). And what of the human analogy of mothers who are adopting infants? Although, among humans, comparisons in brain response patterns between adoptive and non-adoptive parents to infant cues have not been explored, based on the animal work one might predict a pattern of activation in adoptive mothers that is similar to the pattern seen in new mothers. Anecdotal evidence suggests that adoptive parents and are certainly as motivated as biological parents and experience strong positive affect and feelings of attachment. This is certainly true of alloparents (see Hrdy, 2009).

The above discussions are for the most part speculative as there are at this time no discernible

patterns in the imaging literature related to methodology or maternal experience that predict a role for some maternal regions and not others. In mothers, factors have been found to mediate maternal response to infant stimuli, however, including type of delivery (Swain et al., 2008) and adult attachment status (Strathearn et al., 2009). Swain and co-authors (2008) examined the effect of type of delivery on the maternal response to own infant cries compared to an unfamiliar infant cry and temporally matched white-noise. A main rationale behind examining type of delivery was that the experience of childbirth by vaginal delivery (VD) compared with cesarean section delivery (CSD) uniquely involves the release of oxytocin (Swain et al., 2008). Using a similar design to that of Lorberbaum et al. (2002), six CSD and six VD mothers completed a block-design fMRI task 2–4 weeks postpartum. A region-of-interest analysis revealed that in response to their own infant cry compared to an unfamiliar infant cry, VD mothers showed a greater response in a number of regions including the hypothalamus, striatum and amygdala. It was noted that the results for the hypothalamus in particular may highlight its role in mothering and mothering behaviors such as breastfeeding as well as attachment (Swain et al., 2008). In a recent study, Strathearn and colleagues (2009) examined brain response to happy, sad and neutral own and unfamiliar infant faces in mothers whose attachment status was defined as secure or insecure/dismissing. A number of different measures, including questionnaire data, videotaped mother–infant interaction and blood collection for oxytocin sampling, were collected over an approximately one-and-a-half year period. The fMRI session was conducted at seven months postpartum. Their main findings were that compared to insecure/dismissing mothers, securely attached mothers demonstrated significantly more activity in the lateral prefrontal cortex, medial prefrontal cortex and the hypothalamus/pituitary region in response to their own infant faces and greater response in the ventral striatum, orbitofrontal cortex and medial prefrontal cortex in response to own happy infant faces. Interestingly, the authors also found that insecurely/dismissing mothers had greater activity in brain regions associated with negative affect (e.g., the insula) in response to their own infant's sad faces.

These two studies have nicely demonstrated how engagement of a maternal system by infant stimuli is not universal and is in fact influenced by maternal factors and individual differences relevant to mothering. Furthermore, it is likely that individual differences that are related to circuits that overlap with or interact with maternal circuits, such as depression and early experience, may be particularly influential in how a mother's brain responds to her infant.

Although published reports are few at this time, important individual differences in maternal brain

structure and function related to early experience and mood/affect are currently being investigated (e.g., Barrett et al., 2009; Kim et al., 2009b). A recent study by Kim and colleagues examined the relationship between retrospective reports of early maternal care and (1) mother's brain structure (gray matter volume) and (2) maternal brain response to infant cries. In the group of mothers, perceived higher maternal care in childhood was associated with higher gray matter volume in frontal, orbital and temporal cortices (Brodmann areas 10, 47 and 22/20, respectively) as well as greater brain response to infant cries in regions including the DLPFC and temporal cortex. Reports of low maternal care were also related to increased brain response in the hippocampus. The authors suggest that their findings reflect early experience-mediated differences in the ability to understand the infants' mental and physical states (key to sensitive mothering) as well as affective reactivity to cry stimuli.

In our own imaging work, we are examining mothers early in the postpartum period (three months postpartum) and collecting indices of behavioral (coded videotaped mother-infant interaction), affective (depression and anxiety scales, ratings of affective response to infant faces), attitudinal (infant-related), hormonal (cortisol) and neural (BOLD response to positive and negative own and unfamiliar infant faces) responsiveness as well as retrospective accounts of early experience in family of origin (parental bonding, childhood abuse).

Although our work is ongoing, one of our analysis strategies has been to extract brain data (i.e., beta weights derived by the general linear model) from a region of interest (the anterior cingulate cortex) and relate activity in this region to a maternal factor (retrospective reports of early experiences in family of origin, see Barrett et al., 2009). By linking brain structures or circuits to specific maternal factors and examining individual differences, we feel this approach will be helpful in understanding the neurobiology underlying the many components that comprise and influence how mothers mother. To this aim, our preliminary work in 12 mothers suggested that maternal retrospective reports of quality of early experiences related to parental bonding and abuse are significantly related to maternal anterior cingulate cortex response to own baby (compared to unfamiliar baby), where greater magnitude of anterior cingulate cortex response to one's own baby is related to reports of poorer parental bonding (maternal and paternal care) and more emotional abuse (Barrett et al., 2009). It is difficult at this time to know what increased ACC response to one's own infant *means* about the mother and her responsivity or maternal behavior in the context of quality of early experience. In addition, while we may infer that increases in BOLD signal reflect increases in population activity in a given brain region, we are not sure if the activity represents the

inhibition or facilitation of brain process or function. Based on what is known about the function of the ACC, we may speculate that increased response in this region is associated with self- or other-referential thoughts or evaluation, with the simulation of experience, with affective response and/or arousal. Note that all of these processes or states may vary along an affect dimension, having positive, neutral or negative valence. While we may predict that poorer quality of early parental care would be related to the negatively valenced side of things in terms of maternal responsiveness, this suggestion warrants further investigation.

VI. Final integration

The nature of the mother-infant dance is complex and relies on the integrity and function of numerous physiological and behavioral systems in the domains of sensation, perception, affect, reward, executive function, motor output and learning. To engage in mothering behavior, mothers have to be sensitive to infant cues, select those cues for processing and thus such cues must be attractive and salient for the mother. Furthermore, mothers must be emotionally prepared and positively motivated to engage socially with the infant, they must selectively attend to the infant in the context of competing stimuli, and finally, they must be restrained and consistent in their responsiveness. The nature of the mother-infant dance relies on the integrity of multiple physiological and behavioral systems and also on two maternal experiential factors, one proximal and one distal, that have a great impact on how a mother mothers: postpartum depression and early experiences. When a mother is at risk to engage in less than optimal mothering, such as when she is depressed or has experienced adversity in childhood, the function of many or all of maternal and related systems may be affected. In this chapter, we have detailed how mothering is intimately intertwined with affect and the deleterious effects of early experience (e.g., stress systems). The interrelation between maternal, affect and stress systems manifests in many ways. At the behavioral level, maternal affect and quality of early experiences are related to less than optimal attachment relationships, maternal attitudes and mother-infant communication. At the hormonal level, the neurobiology of these systems is strikingly similar. Furthermore, it is likely that the similarity and cross-talk between maternal affect and stress systems also allows for mood disturbance and early adverse experiences to have a significant impact on the quality of mothering and the motivation to mother.

The main purpose of this discussion was to extend what is known about the neurobiology of mothering to functional neuroimaging. Instead of focusing on strictly 'maternal' studies, we instead

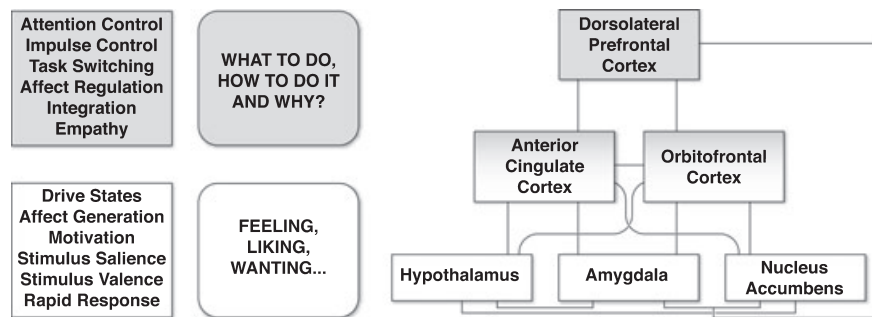


Figure 3 Schematic of a putative human maternal circuit. Brain regions known or believed to be important in human maternal behavior serve a number of important functions. There are (relatively) gross subcortical functions related to reward, affect and motivation that serve to ensure that the baby is a strongly positively reinforcing stimulus that the mother is driven to care for, to be responsive to and show affection to. There are also higher-order cortical functions that regulate maternal behavior in the context of the (internal and external) environment and in light of over-arching goals, standards, mores and intentions. Note that some regions, namely the anterior cingulate cortex and orbitofrontal cortex, operate at the interface of the two main systems

used a systems approach to survey important findings relevant to brain systems integral to and/or strongly related to the mothering experience: (a) social behavior; (b) reward and affect; (c) executive function; and (d) maternal behavior. In human neuroscience, without ablation techniques, microdialysis or electrical stimulation, direct brain-behavior relationships are difficult to nail down and we must often extrapolate and speculate. We have seen that this is especially challenging when examining something as complex as human maternal behavior. However, by examining each of our systems of interest in the context of maternal behavior, it becomes easier to envision the function of each region in our putative maternal circuit (see Figure 3). Furthermore, we find that there are many commonalities in terms of the brain regions identified across these systems and, as we would expect, all are sensitive to the influence of, or function differently in the context of, depression and adverse early experience. So, in addition to the behavioral and hormonal findings, we have identified another mechanism by which individual differences can impact the quality of mothering. Key to progress in mapping the maternal brain will be discovering and accounting for important individual differences that influence brain regions important in mothering and determining whether or not some circuits/regions are influenced more than others and how, in other words, to identify specific structure-function relationships in the context of maternal behavior. As often observed in studies of behavior and hormones, all mothers are not created equal and brain differences should, in part, reflect this.

To conclude then, although we have learned a great deal about the psychobiology of mothering over the past 20 years, there is still much to learn and much to revisit, given new knowledge. No discussion on individual differences is complete

without reference to genetics and their impact on the variety of ways the environment is expressed in mothers' behavior (Bakermans-Kranenburg & Van IJzendoorn, 2008). Some mothers are attentive, others not; some mothers are affectively attached, others not. Some mothers are predominantly talkers; others are quieter but interact through stroking and touching; others avoid or evade. And mothers differ enormously from one another in their temperaments, their hormones, and their brains. These individual differences cannot be entirely explained by knowing the early environment in which mothers were reared, or by knowing the present social context or affective state in which the mother finds herself.

The notions of psychological resilience in face of adversity and of susceptibility to positive effects of 'good' early experience bring with them questions about the mother's genotype and how polymorphisms in specific genes and gene sets interact with early and present experience to help create the vast differences in temperament, affect, reward susceptibility, sensitivity and executive function capabilities necessary for mothers to mother effectively. This next decade, when we use what we have learned about the genome to better understand behavior and brain, should be a very exciting time for the study of the psychobiology of mothering.

Correspondence to

Jennifer Barrett, Department of Psychology, University of Toronto at Mississauga, South Building, Room 2037B, 3359 Mississauga Rd. N., Mississauga, ON N5L 1C6, Canada; Tel: 905-569-4292; Email: jennifer.a.barrett@mail.mcgill.ca; or Alison S. Fleming, Department of Psychology, University of Toronto at Mississauga; Tel: 905-828-3961; Email: alison.fleming@utoronto.ca

Key points

- Mothering behavior and feelings are a product of a wide variety of behavioral and physiological propensities and underlying systems.
- Quality of mothering relies on maternal factors, one proximal and one distal, that have an impact on how a mother mothers: postpartum depression and adverse (stressful) early experiences.
- The brain mechanisms that regulate mothering include modules or systems within the hypothalamus, the limbic system and the cortex; these systems are interrelated and are sensitive to the influence of, or function differently in the context of, variations in maternal mood and early experiences in family of origin.
- In future work, the study of functional, molecular and gene expression changes in the brain that occur under different environmental contexts and/or that vary with genotype may help us to understand why mothers differ from one another in the extent to which their mothering and postpartum mood state is affected by adverse early experiences and stresses in their lives.

References

- Abdulrazzaq, Y.M., Al Kendi, A., & Nagelkerke, N. (2009). Soothing methods used to calm a baby in an Arab country. *Acta Paediatrica*, 98, 392–396.
- Afonso, V.M., Grella, S.L., Chatterjee, D., & Fleming, A.S. (2008). Previous maternal experience affects accumbal dopaminergic responses to pup-stimuli. *Brain Research*, 1198, 115–123.
- Afonso, V.M., King, S., Chatterjee, D., & Fleming, A.S. (2009). Hormones that increase maternal responsiveness affect accumbal dopaminergic responses to pup- and food-stimuli in the female rat. *Hormones and Behavior*, 56, 11–23.
- Afonso, V.M., Sison, M., Lovic, V., & Fleming, A.S. (2007). Medial prefrontal cortex lesions in the female rat affect sexual and maternal behavior and their sequential organization. *Behavioral Neuroscience*, 121, 515–526.
- Ainsworth, M., Bell, S., & Stayton, D. (1974). Infant-mother attachment and social development: Socialization of reciprocal responsiveness to signals. In M. Richards (Ed.), *The integration of a child into a social world* (pp. 99–135). Cambridge: Cambridge University Press.
- Anisfeld, E., Casper, V., Nozyce, M., & Cunningham, N. (1990). Does infant carrying promote attachment? An experimental study of the effects of increased physical contact on the development of attachment. *Child Development*, 61, 1617–1627.
- Arnott, B., & Meins, E. (2007). Links among antenatal attachment representations, postnatal mind-mindedness, and infant attachment security: A preliminary study of mothers and fathers. *Bulletin of the Menninger Clinic*, 71, 132–149.
- Aron, A., Fisher, H., Mashek, D.J., Strong, G., Li, H., & Brown, L.L. (2005). Reward, motivation, and emotion systems associated with early-stage intense romantic love. *Journal of Neurophysiology*, 94, 327–337.
- Atkinson, L., Leung, E., Goldberg, S., Benoit, D., Poulton, L., Myhal, N., et al. (2009). Attachment and selective attention: Disorganization and emotional Stroop reaction time. *Development and Psychopathology*, 21, 99–126.
- Bakermans-Kranenburg, M.J., & van IJzendoorn, M.H. (2008). Oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes associated with observed parenting. *Social Cognitive and Affective Neuroscience*, 3, 128–134.
- Banasr, M., Valentine, G.W., Li, X., Gourley, S.L., Taylor, J.R., & Duman, R.S. (2007). Chronic unpredictable stress decreases cell proliferation in the cerebral cortex of the adult rat. *Biological Psychiatry*, 62, 496–504.
- Banki, C.M., Bissette, G., Arato, M., O'Connor, L., & Nemeroff, C.B. (1987). CSF corticotropin-releasing factor-like immunoreactivity in depression and schizophrenia. *The American Journal of Psychiatry*, 144, 873–877.
- Banki, C.M., Karmacs, L., Bissette, G., & Nemeroff, C.B. (1992). Cerebrospinal fluid neuropeptides in mood disorder and dementia. *Journal of Affective Disorders*, 25, 39–45.
- Barch, D.M., Braver, T.S., Sabb, F.W., & Noll, D.C. (2000). Anterior cingulate and the monitoring of response conflict: Evidence from an fMRI study of overt verb generation. *Journal of Cognitive Neuroscience*, 12, 298–309.
- Barrett, J., & Armony, J.L. (2009). Influence of trait anxiety on brain activity during the acquisition and extinction of aversive conditioning. *Psychological Medicine*, 39, 255–265.
- Barrett, J., Hall, G., Wonch, K., Ali, N., Gonzalez, A., Steiner, M., et al. (2009). Quality of early parental care reported by mothers is related to anterior cingulate response to own infant stimuli: Preliminary findings. *NeuroImage*, 47, S181–S181.
- Bartels, A., & Zeki, S. (2000). The neural basis of romantic love. *Neuroreport*, 11, 3829–3834.
- Bartels, A., & Zeki, S. (2004). The neural correlates of maternal and romantic love. *NeuroImage*, 21, 1155–1166.
- Beebe, B., Badalamenti, A., Jaffe, J., Feldstein, S., Marquette, L., Helbraun, E., et al. (2008). Distressed mothers and their infants use a less efficient timing mechanism in creating expectancies of each other's looking patterns. *Journal of Psycholinguistic Research*, 37, 293–307.
- Belsky, J. (1984). The determinants of parenting: A process model. *Child Development*, 55, 83–96.
- Benoit, D., & Parker, K.C. (1994). Stability and transmission of attachment across three generations. *Child Development*, 65, 1444–1456.
- Bergman, K., Sarkar, P., Glover, V., & O'Connor, T.G. (in press). Maternal prenatal cortisol and infant cognitive development: Moderation by infant-mother attachment. *Biological Psychiatry*.
- Bernet, C.Z., & Stein, M.B. (1999). Relationship of childhood maltreatment to the onset and course of major

- depression in adulthood. *Depression and Anxiety*, 9, 169–174.
- Bernstein, I.H., Rush, A.J., Yonkers, K., Carmody, T.J., Woo, A., McConnell, K., et al. (2008). Symptom features of postpartum depression: Are they distinct? *Depression and Anxiety*, 25, 20–26.
- Bifulco, A., Kwon, J., Jacobs, C., Moran, P. M., Bunn, A., & Beer, N. (2006). Adult attachment style as mediator between childhood neglect/abuse and adult depression and anxiety. *Social Psychiatry and Psychiatric Epidemiology*, 41, 796–805.
- Bifulco, A., Moran, P.M., Baines, R., Bunn, A., & Stanford, K. (2002). Exploring psychological abuse in childhood: II. Association with other abuse and adult clinical depression. *Bulletin of the Menninger Clinic*, 66, 241–258.
- Blakemore, S.J., & Decety, J. (2001). From the perception of action to the understanding of intention. *Nature Reviews. Neuroscience*, 2, 561–567.
- Bornstein, M.H., Tamis-LeMonda, C.S., Hahn, C., & Haynes, O.M. (2008). Maternal responsiveness to young children at three ages: Longitudinal analysis of a multidimensional, modular, and specific parenting construct. *Developmental Psychology*, 44, 867–874.
- Bos, K.J., Fox, N., Zeanah, C.H., & Nelson, C.A. III (2009). Effects of early psychosocial deprivation on the development of memory and executive function. *Frontiers in Behavioral Neuroscience*, 3, 16.
- Boyce, P.M., & Todd, A.L. (1992). Increased risk of postnatal depression after emergency caesarean section. *The Medical Journal of Australia*, 157, 172–174.
- Brand, S.R., & Brennan, P.A. (2009). Impact of antenatal and postpartum maternal mental illness: How are the children? *Clinical Obstetrics and Gynecology*, 52, 441–455.
- Brazelton, T.B. (1977). Implications of infant development among Mayan Indians of Mexico. In P.H. Leiderman, S.R. Tulkin, & A. Rosenfeld (Eds.), *Culture and infancy: Variations in the human experience* (pp. 151–188). New York: Academic Press.
- Bremner, J.D., Elzinga, B., Schmahl, C., & Vermetten, E. (2008). Structural and functional plasticity of the human brain in posttraumatic stress disorder. *Progress in Brain Research*, 167, 171–186.
- Bridges, R. (2008). *Neurobiology of the parental brain*. Amsterdam: Academic.
- Bridges, R.S. (1990). Endocrine regulation of parental behavior in rodents. In N.A. Krasnegor, & R.S. Bridges (Eds.), *Mammalian parenting: Biochemical, neurobiological, and behavioral determinants* (pp. 93–117). New York: Oxford University Press.
- Brown, G.W., & Moran, P. (1994). Clinical and psychosocial origins of chronic depressive episodes. I: A community survey. *British Journal of Psychiatry*, 165, 447–456.
- Brown, J., Cohen, P., Johnson, J.G., & Smailes, E.M. (1999). Childhood abuse and neglect: Specificity of effects on adolescent and young adult depression and suicidality. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38, 1490–1496.
- Brown, J.W., & Braver, T.S. (2005). Learned predictions of error likelihood in the anterior cingulate cortex. *Science*, 307, 1118–1121.
- Brown, J.W., & Braver, T.S. (2008). A computational model of risk, conflict, and individual difference effects in the anterior cingulate cortex. *Brain Research*, 1202, 99–108.
- Buist, A. (2006). Perinatal depression – assessment and management. *Australian Family Physician*, 35, 670–673.
- Burton, C., Lovic, V., & Fleming, A.S. (2006). Early adversity alters attention and locomotion in adult Sprague–Dawley rats. *Behavioral Neuroscience*, 120, 665–675.
- Burton, C.L., Chatterjee, D., Chatterjee-Chakraborty, M., Lovic, V., Grella, S.L., Steiner, M., et al. (2007). Prenatal restraint stress and motherless rearing disrupts expression of plasticity markers and stress-induced corticosterone release in adult female Sprague–Dawley rats. *Brain Research*, 1158, 28–38.
- Carmichael, S.T., & Price, J.L. (1994). Architectonic subdivision of the orbital and medial prefrontal cortex in the macaque monkey. *Journal of Comparative Neurology*, 346, 366–402.
- Carpenter, L.L., Tyrka, A.R., McDougale, C.J., Malison, R.T., Owens, M.J., Nemeroff, C.B., et al. (2004). Cerebrospinal fluid corticotropin-releasing factor and perceived early-life stress in depressed patients and healthy control subjects. *Neuropsychopharmacology*, 29, 777–784.
- Carter, R.M., Macinnes, J.J., Huettel, S.A., & Adcock, R.A. (2009). Activation in the VTA and nucleus accumbens increases in anticipation of both gains and losses. *Frontiers in Behavioral Neuroscience*, 3, 21.
- Champagne, F., & Meaney, M.J. (2001). Like mother, like daughter: Evidence for non-genomic transmission of parental behavior and stress responsivity. *Progress in Brain Research*, 133, 287–302.
- Champagne, F.A., Chretien, P., Stevenson, C.W., Zhang, T.Y., Gratton, A., & Meaney, M.J. (2004). Variations in nucleus accumbens dopamine associated with individual differences in maternal behavior in the rat. *Journal of Neuroscience*, 24, 4113–4123.
- Champagne, F.A., Francis, D.D., Mar, A., & Meaney, M.J. (2003). Variations in maternal care in the rat as a mediating influence for the effects of environment on development. *Physiology and Behavior*, 79, 359–371.
- Chatterjee, D., Chatterjee-Chakraborty, M., Rees, S., Cauchi, J., de Medeiros, C.B., & Fleming, A.S. (2007). Maternal isolation alters the expression of neural proteins during development: ‘Stroking’ stimulation reverses these effects. *Brain Research*, 1158, 11–27.
- Chaudron, L.H., Kitzman, H.J., Peifer, K.L., Morrow, S., Perez, L.M., & Newman, M.C. (2005). Self-recognition of and provider response to maternal depressive symptoms in low-income Hispanic women. *Journal of Women’s Health*, 14, 331–338.
- Chisholm, J.S. (1978). Swaddling, cradleboards and the development of children. *Early Human Development*, 2, 255–275.
- Christoff, K., Keramati, K., Gordon, A.M., Smith, R., & Mädlar, B. (2009). Prefrontal organization of cognitive control according to levels of abstraction. *Brain Research*, 1286, 94–105.
- Cicchetti, D., Rogosch, F.A., & Toth, S.L. (1998). Maternal depressive disorder and contextual risk: Contributions to the development of attachment insecurity and behavior problems in toddlerhood. *Development and Psychopathology*, 10, 283–300.
- Clark, L., Chamberlain, S.R., & Sahakian, B.J. (2009). Neurocognitive mechanisms in depression: Implications for treatment. *Annual Review of Neuroscience*, 32, 57–74.
- Cohn, J.F., Campbell, S.B., Matias, R., & Hopkins, J. (1990). Face-to-face interactions of postpartum depressed and nondepressed mother–infant pairs at 2 months. *Developmental Psychology*, 35, 119–123.
- Cole, M.W., & Schneider, W. (2007). The cognitive control network: Integrated cortical regions with dissociable functions. *NeuroImage*, 37, 343–360.

- Cooper, J.C., & Knutson, B. (2008). Valence and salience contribute to nucleus accumbens activation. *NeuroImage*, 39, 538–547.
- Cooper, P.J., & Murray, L. (1995). Course and recurrence of postnatal depression. Evidence for the specificity of the diagnostic concept. *British Journal of Psychiatry*, 166, 191–195.
- Coplan, J.D., Andrews, M.W., Rosenblum, L.A., Owens, M.J., Friedman, S., Gorman, J.M., et al. (1996). Persistent elevations of cerebrospinal fluid concentrations of corticotropin-releasing factor in adult nonhuman primates exposed to early-life stressors: Implications for the pathophysiology of mood and anxiety disorders. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 1619–1623.
- Cortez, C., & Fleming, A.S. (1990). Maternal responsiveness in humans: Emotional, cognitive and biological factors. *Advances in the Study of Behavior*, 19, 83–136.
- Cortez, C., & Fleming, A.S. (2002). Psychobiology of maternal behavior in human beings. In M.H. Bornstein (Ed.), *Handbook of parenting: Biology and ecology of parenting* (pp. 141–182). Mahwah, NJ: Lawrence Erlbaum Associates.
- Cote, L.R., & Bornstein, M.H. (2009). Child and mother play in three US cultural groups: Comparisons and associations. *Journal of Family Psychology*, 23, 355–363.
- Cox, J.L., Murray, D., & Chapman, G. (1993). A controlled study of the onset, duration and prevalence of postnatal depression. *British Journal of Psychiatry*, 163, 27–31.
- Critchley, H.D. (2009). Psychophysiology of neural, cognitive and affective integration: fMRI and autonomic indicants. *International Journal of Psychophysiology*, 73, 88–94.
- Dannlowski, U., Ohrmann, P., Bauer, J., Deckert, J., Hohoff, C., Kugel, H., et al. (2008). 5-HTTLPR biases amygdala activity in response to masked facial expressions in major depression. *Neuropsychopharmacology*, 33, 418–424.
- Dannlowski, U., Ohrmann, P., Bauer, J., Kugel, H., Arolt, V., Heindel, W., et al. (2007). Amygdala reactivity to masked negative faces is associated with automatic judgmental bias in major depression: A 3 T fMRI study. *Journal of Psychiatry and Neuroscience*, 32, 423–429.
- Davey, C.G., Allen, N.B., Harrison, B.J., Dwyer, D.B., & Yücel, M. (2009). Being liked activates primary reward and midline self-related brain regions. *Human Brain Mapping*, 31, 660–668.
- De Bellis, M.D. (2005). The psychobiology of neglect. *Child Maltreatment*, 10, 150–172.
- Debiec, J. (2005). Peptides of love and fear: Vasopressin and oxytocin modulate the integration of information in the amygdala. *BioEssays*, 27, 869–873.
- de Paül, J., & Domenech, L. (2000). Childhood history of abuse and child abuse potential in adolescent mothers: a longitudinal study. *Child Abuse & Neglect*, 24(5), 701–713.
- Derntl, B., Habel, U., Windischberger, C., Robinson, S., Kryspin-Exner, I., Gur, R.C., et al. (2009). General and specific responsiveness of the amygdala during explicit emotion recognition in females and males. *BMC Neuroscience*, 10, 91.
- Di Chiara, G. (2002). Nucleus accumbens shell and core dopamine: Differential role in behavior and addiction. *Behavioural Brain Research*, 137, 75–114.
- Dichter, G.S., Felder, J.N., & Smoski, M.J. (2009). Affective context interferes with cognitive control in unipolar depression: An fMRI investigation. *Journal of Affective Disorders*, 114, 131–142.
- Dillon, D.G., Holmes, A.J., Birk, J.L., Brooks, N., Lyons-Ruth, K., & Pizzagalli, D.A. (2009). Childhood adversity is associated with left basal ganglia dysfunction during reward anticipation in adulthood. *Biological Psychiatry*, 66, 206–213.
- Drevets, W.C., Price, J.L., & Furey, M.L. (2008). Brain structural and functional abnormalities in mood disorders: Implications for neurocircuitry models of depression. *Brain Structure and Function*, 213, 93–118.
- Drevets, W.C., Savitz, J., & Trimble, M. (2008b). The subgenual anterior cingulate cortex in mood disorders. *CNS Spectrums*, 13, 663–681.
- Duncan, J., & Owen, A.M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, 23, 475–483.
- Elliott, R., Sahakian, B.J., McKay, A.P., Herrod, J.J., Robbins, T.W., & Paykel, E.S. (1996). Neuropsychological impairments in unipolar depression: The influence of perceived failure on subsequent performance. *Psychological Medicine*, 26, 975–989.
- Enns, M.W., Cox, B.J., & Clara, I. (2002). Parental bonding and adult psychopathology: Results from the US National Comorbidity Survey. *Psychological Medicine*, 32, 997–1008.
- Fahlke, C., Lorenz, J.G., Long, J., Champoux, M., Suomi, S.J., & Higley, J.D. (2000). Rearing experiences and stress-induced plasma cortisol as early risk factors for excessive alcohol consumption in nonhuman primates. *Alcoholism, Clinical and Experimental Research*, 24, 644–650.
- Feldman, R., Granat, A., Pariente, C., Kanety, H., Kuint, J., & Gilboa-Schechtman, E. (2009). Maternal depression and anxiety across the postpartum year and infant social engagement, fear regulation, and stress reactivity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 48, 919–927.
- Feldman, R., Weller, A., Zagoory-Sharon, O., & Levine, A. (2007). Evidence for a neuroendocrinological foundation of human affiliation: Plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. *Psychological Science*, 18, 965–970.
- Field, T. (1995). Psychologically depressed parents. In M. Bernstein (Ed.), *Handbook of parenting*. Mahwah, NJ: Lawrence Erlbaum Associates.
- Field, T. (2009). Postpartum depression effects on early interactions, parenting, and safety practices: A review. *Infant Behavior and Development*, 33, 1–6.
- Field, T., Diego, M., Hernandez-Reif, M., Schanberg, S., & Kuhn, C. (2002). Right frontal EEG and pregnancy/neonatal outcomes. *Psychiatry*, 65, 35–47.
- Field, T., Healy, B., Goldstein, S., & Guthertz, M. (1990). Behavior-state matching and synchrony in mother-infant interactions of versus depressed dyads. *Developmental Psychology*, 26, 7–14.
- Field, T., Hernandez-Reif, M., Diego, M., Feijo, L., Vera, Y., Gil, K., et al. (2007). Still-face and separation effects on depressed mother-infant interactions. *Infant Mental Health Journal*, 28, 314–323.
- Field, T., Sandberg, D., Garcia, R., Bega-Lahr, N., Goldstein, S., & Guy, L. (1985). Pregnancy problems, postpartum depression, and early mother-infant interactions. *Developmental Psychobiology*, 21, 1152–1156.
- Figueira, P., Fernandes Malloy-Diniz, L., Aurélio Romano-Silva, M., Silva Neves, F., & Corrêa, H. (2009). Postpartum depression and comorbid disorders: Frequency

- and relevance to clinical management. *Archives of Women's Mental Health*, 12, 451.
- Fineberg, N.A., Potenza, M.N., Chamberlain, S.R., Berlin, H.A., Menzies, L., Bechara, A., Sahakian, B.J., et al. (2010). Probing compulsive and impulsive behaviors, from animal models to endophenotypes: A narrative review. *Neuropsychopharmacology*, 35, 591–604.
- Fishbein, D., Warner, T., Krebs, C., Trevarthen, N., Flannery, B., & Hammond, J. (2009). Differential relationships between personal and community stressors and children's neurocognitive functioning. *Child Maltreatment*, 14, 299–315.
- Fisher, H., Aron, A., & Brown, L.L. (2005). Romantic love: An fMRI study of a neural mechanism for mate choice. *Journal of Comparative Neurology*, 493, 58–62.
- Fleming, A.S., Corter, C., Franks, P., Surbey, M., Schneider, B., & Steiner, M. (1993). Postpartum factors related to mother's attraction to newborn infant odors. *Developmental Psychobiology*, 26, 115–132.
- Fleming, A.S., & Korsmit, M. (1996). Plasticity in the maternal circuit: Effects of maternal experience on Fos-lir in hypothalamic, limbic and cortical structures in the postpartum rat. *Behavioral Neuroscience*, 110, 567–582.
- Fleming, A.S., Kraemer, G.W., Gonzalez, A., Lovic, V., Rees, S., & Melo, A. (2002). Mothering begets mothering: The transmission of behavior and its neurobiology across generations. *Pharmacology, Biochemistry, and Behavior*, 73, 61–75.
- Fleming, A.S., & Rosenblatt, J.S. (1974a). Olfactory regulation of maternal behavior in rats. I. Effects of olfactory bulb removal in experienced and inexperienced lactating and cycling females. *Journal of Comparative and Physiological Psychology*, 86, 221–232.
- Fleming, A.S., & Rosenblatt, J.S. (1974b). Olfactory regulation of maternal behavior in rats. II. Effects of peripherally induced anosmia and lesions of the lateral olfactory tract in pup-induced virgins. *Journal of Comparative and Physiological Psychology*, 86, 233–246.
- Fleming, A.S., Ruble, D.N., Flett, G.L., & Shaul, D. (1988). Postpartum adjustment in first-time mothers: Relations between mood, maternal attitudes and mother–infant interactions. *Developmental Psychology*, 24, 71–81.
- Fleming, A.S., Ruble, D., Krieger, H., & Wong, P.Y. (1997a). Hormonal and experiential correlates of maternal responsiveness during pregnancy and the puerperium in human mothers. *Hormones and Behavior*, 31, 145–158.
- Fleming, A.S., Steiner, M., & Anderson, V. (1987). Hormonal and attitudinal correlates of maternal behavior during the early postpartum pregnancy. *Journal of Reproductive and Infant Psychology*, 5, 193–205.
- Fleming, A.S., Steiner, M., & Corter, C. (1997b). Cortisol, hedonics, and maternal responsiveness in human mothers. *Hormones and Behavior*, 32, 85–98.
- Fossati, P., Ergis, A.M., & Allilaire, J.F. (2001). Problem-solving abilities in unipolar depressed patients: Comparison of performance on the modified version of the Wisconsin and the California sorting tests. *Psychiatry Research*, 104, 145–156.
- France, R.D., Urban, B., Krishnan, K.R., Bissette, G., Banki, C.M., Nemeroff, C., et al. (1988). CSF corticotropin-releasing factor-like immunoactivity in chronic pain patients with and without major depression. *Biological Psychiatry*, 23, 86–88.
- Francis, D., Diorio, J., Liu, D., & Meaney, M.J. (1999). Nongenomic transmission across generations of maternal behavior and stress responses in the rat. *Science*, 286, 1155–1158.
- Friedman, S.H., & Resnick, P.J. (2009). Postpartum depression: An update. *Women's Health*, 5, 287–295.
- Fu, C.H.Y., Williams, S.C.R., Cleare, A.J., Scott, J., Mitterschiffthaler, M.T., Walsh, N.D., et al. (2008). Neural responses to sad facial expressions in major depression following cognitive behavioral therapy. *Biological Psychiatry*, 64, 505–512.
- Fujiwara, J., Tobler, P.N., Taira, M., Iijima, T., & Tsutsui, K. (2009). Segregated and integrated coding of reward and punishment in the cingulate cortex. *Journal of Neurophysiology*, 101, 3284–3293.
- Furstenberg, F.F., Brooks-Gunn, J., & Morgan, S.P. (1987). Adolescent mothers and their children in later life. *Family Planning Perspectives*, 19, 142–151.
- Gale, S., & Harlow, B.L. (2003). Postpartum mood disorders: A review of clinical and epidemiological factors. *Journal of Psychosomatic Obstetrics and Gynaecology*, 24, 257–266.
- Gamer, M., & Büchel, C. (2009). Amygdala activation predicts gaze toward fearful eyes. *Journal of Neuroscience*, 29, 9123–9126.
- Garner, B., Wood, S.J., Pantelis, C., & van den Buuse, M. (2007). Early maternal deprivation reduces prepulse inhibition and impairs spatial learning ability in adulthood: No further effect of post-pubertal chronic corticosterone treatment. *Behavioural Brain Research*, 176, 323–332.
- Gavin, N.I., Gaynes, B.N., Lohr, K.N., Meltzer-Brody, S., Gartlehner, G., & Swinson, T. (2005). Perinatal depression: A systematic review of prevalence and incidence. *Obstetrics and Gynecology*, 106(5 Pt 1), 1071–1083.
- Giacobbe, P., Mayberg, H.S., & Lozano, A.M. (2009). Treatment resistant depression as a failure of brain homeostatic mechanisms: Implications for deep brain stimulation. *Experimental Neurology*, 219, 44–52.
- Giardino, J., Gonzalez, A., Steiner, M., & Fleming, A.S. (2008). Effects of motherhood on physiological and subjective responses to infant cries in teenage mothers: A comparison with non-mothers and adult mothers. *Hormones and Behavior*, 53, 149–158.
- Glocker, M.L., Langleben, D.D., Ruparel, K., Loughead, J.W., Valdez, J.N., Griffin, M.D., et al. (2009). Baby schema modulates the brain reward system in nulliparous women. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 9115–9119.
- Gobbini, M.I., & Haxby, J.V. (2007). Neural systems for recognition of familiar faces. *Neuropsychologia*, 45, 32–41.
- Goldstone, A.P., de Hernandez, C.G.P., Beaver, J.D., Muhammed, K., Croese, C., Bell, G., et al. (2009). Fasting biases brain reward systems towards high-calorie foods. *European Journal of Neuroscience*, 30, 1625–1635.
- Gonzalez, A., & Fleming, A.S. (2002). Artificial rearing causes changes in maternal behavior and c-fos expression in juvenile female rats. *Behavioral Neuroscience*, 116, 999–1013.
- Gonzalez, A., Jenkins, J.M., Steiner, M., & Fleming, A.S. (2009). The relation between early life adversity, cortisol awakening response and diurnal salivary cortisol levels in postpartum women. *Psychoneuroendocrinology*, 34, 76–86.
- Gonzalez, A., Lovic, V., Ward, G.R., Wainwright, P.E., & Fleming, A.S. (2001). Intergenerational effects of complete maternal deprivation and replacement stimulation on maternal behavior and emotionality in female rats. *Developmental Psychobiology*, 38, 11–32.
- Goto, Y., & Grace, A.A. (2005). Dopamine-dependent interactions between limbic and prefrontal cortical plas-

- ticity in the nucleus accumbens: Disruption by cocaine sensitization. *Neuron*, 47, 255–266.
- Goto, Y., & Grace, A.A. (2008). Limbic and cortical information processing in the nucleus accumbens. *Trends in Neurosciences*, 31, 552–558.
- Goyal, D., Gay, C., & Lee, K. (2009). Fragmented maternal sleep is more strongly correlated with depressive symptoms than infant temperament at three months postpartum. *Archives of Women's Mental Health*, 12, 229–237.
- Grabenhorst, F., Rolls, E.T., Parris, B.A., & d'Souza, A.A. (2009). How the brain represents the reward value of fat in the mouth. *Cerebral Cortex*, 20, 1082–1091.
- Grant, M.M., Thase, M.E., & Sweeney, J.A. (2001). Cognitive disturbance in outpatient depressed younger adults: Evidence of modest impairment. *Biological Psychiatry*, 50, 35–43.
- Gray, J., Venn, H., Montagne, B., Murray, L., Burt, M., Frigerio, E., et al. (2006). Bipolar patients show mood-congruent biases in sensitivity to facial expressions of emotion when exhibiting depressed symptoms, but not when exhibiting manic symptoms. *Cognitive Neuropsychiatry*, 11, 505–520.
- Groër, M.W., & Morgan, K. (2007). Immune, health and endocrine characteristics of depressed postpartum mothers. *Psychoneuroendocrinology*, 32, 133–139.
- Gump, B.B., Reihman, J., Stewart, P., Lonky, E., Darvill, T., Granger, D.A., et al. (2009). Trajectories of maternal depressive symptoms over her child's life span: Relation To adrenocortical, cardiovascular, and emotional functioning in children. *Development and Psychopathology*, 21, 207–225.
- Güngör, D., & Bornstein, M.H. (in press). Culture-general and -specific associations of attachment avoidance and anxiety with perceived parental warmth and psychological control among Turk and Belgian adolescents. *Journal of Adolescence*.
- Gunnar, M.R., Brodersen, L., Nachmias, M., Buss, K., & Rigatuso, J. (1996). Stress reactivity and attachment security. *Developmental Psychobiology*, 29, 191–204.
- Gunnar, M.R., & Fisher, P.A. (2006). Bringing basic research on early experience and stress neurobiology to bear on preventive interventions for neglected and maltreated children. *Development and Psychopathology*, 18, 651–677.
- Halligan, S.L., Murray, L., Martins, C., & Cooper, P.J. (2007). Maternal depression and psychiatric outcomes in adolescent offspring: A 13-year longitudinal study. *Journal of Affective Disorders*, 97, 145–154.
- Harkness, K.L., & Monroe, S.M. (2002). Childhood adversity and the endogenous versus nonendogenous distinction in women with major depression. *American Journal of Psychiatry*, 159, 387–393.
- Heim, C., & Nemeroff, C.B. (1999). The impact of early adverse experiences on brain systems involved in the pathophysiology of anxiety and affective disorders. *Biological Psychiatry*, 46, 1509–1522.
- Heim, C., Plotsky, P.M., & Nemeroff, C.B. (2004). Importance of studying the contributions of early adverse experience to neurobiological findings in depression. *Neuropsychopharmacology*, 29, 641–648.
- Hercher, C., Turecki, G., & Mechawar, N. (2009). Through the looking glass: Examining neuroanatomical evidence for cellular alterations in major depression. *Journal of Psychiatric Research*, 43, 947–961.
- Herrenkohl, T.I., Kosterman, R., Mason, W.A., Hawkins, J.D., McCarty, C.A., & McCauley, E. (2010). Effects of childhood conduct problems and family adversity on health, health behaviors, and service use in early adulthood: Tests of developmental pathways involving adolescent risk taking and depression. *Development and Psychopathology*, 22, 655–665.
- Higley, J.D., Suomi, S.J., & Linnoila, M. (1991). CSF monoamine metabolite concentrations vary according to age, rearing, and sex, and are influenced by the stressor of social separation in rhesus monkeys. *Psychopharmacology*, 103, 551–556.
- Higley, J.D., Suomi, S.J., & Linnoila, M. (1992). A longitudinal assessment of CSF monoamine metabolite and plasma cortisol concentrations in young rhesus monkeys. *Biological Psychiatry*, 32, 127–145.
- Hollerman, J.R., Tremblay, L., & Schultz, W. (2000). Involvement of basal ganglia and orbitofrontal cortex in goal-directed behavior. *Progress in Brain Research*, 126, 193–215.
- Horn, N.R., Dolan, M., Elliott, R., Deakin, J.F.W., & Woodruff, P.W.R. (2003). Response inhibition and impulsivity: An fMRI study. *Neuropsychologia*, 41, 1959–1966.
- Hrdy, S. (2009). *Mothers and others: The evolutionary origins of mutual understanding*. Cambridge MA: Belknap Press of Harvard University Press.
- Hrdy, S.B. (2005). Evolutionary context of human development: The cooperative breeding model. In C.S. Carter, L. Anhalt, K. E. Grossmann, S.B. Hrdy, M.E. Lamb, S.W. Porges, & N. Sachser (Eds.), *Attachment and bonding: A new synthesis* (pp. 9–32). Cambridge, MA: MIT Press.
- Huber, D., Veinante, P., & Stoop, R. (2005). Vasopressin and oxytocin excite distinct neuronal populations in the central amygdala. *Science*, 308, 245–248.
- Insel, T. (1990). Oxytocin and maternal behavior. In N.A. Krasnegor, & R.S. Bridges (Eds.), *Mammalian parenting: Biochemical, neurobiological, and behavioral determinants* (pp. 260–280). New York: Oxford University Press.
- Inoue, Y., Tonooka, Y., Yamada, K., & Kanba, S. (2004). Deficiency of theory of mind in patients with remitted mood disorder. *Journal of Affective Disorders*, 82, 403–409.
- Inoue, Y., Yamada, K., & Kanba, S. (2006). Deficit in theory of mind is a risk for relapse of major depression. *Journal of Affective Disorders*, 95, 125–127.
- Jaffee, S.R., Caspi, A., Moffitt, T.E., Polo-Tomás, M., & Taylor, A. (2007). Individual, family, and neighborhood factors distinguish resilient from non-resilient maltreated children: A cumulative stressors model. *Child Abuse and Neglect*, 31, 231–253.
- Johansen-Berg, H., Gutman, D.A., Behrens, T.E.J., Matthews, P.M., Rushworth, M.F.S., Katz, E., et al. (2008). Anatomical connectivity of the subgenual cingulate region targeted with deep brain stimulation for treatment-resistant depression. *Cerebral Cortex*, 18, 1374–1383.
- Jolley, S.N., Elmore, S., Barnard, K.E., & Carr, D.B. (2007). Dysregulation of the hypothalamic-pituitary-adrenal axis in postpartum depression. *Biological Research for Nursing*, 8, 210–222.
- Kammerer, M., Taylor, A., & Glover, V. (2006). The HPA axis and perinatal depression: A hypothesis. *Archives of Women's Mental Health*, 9, 187–196.
- Kaneda, Y. (2009). Verbal working memory impairment in patients with current episode of unipolar major depressive disorder and in remission. *Clinical Neuropharmacology*, 32, 346–347.
- Kannan, S., Carruth, B.R., & Skinner, J. (2004). Neonatal feeding practices of Anglo American mothers and Asian Indian mothers living in the United States and India. *Journal of Nutrition Education and Behavior*, 36, 315–319.

- Karevold, E., Røysamb, E., Ystrom, E., & Mathiesen, K.S. (2009). Predictors and pathways from infancy to symptoms of anxiety and depression in early adolescence. *Developmental Psychology*, 45, 1051–1060.
- Kaufman, J., Plotsky, P.M., Nemeroff, C.B., & Charney, D.S. (2000). Effects of early adverse experiences on brain structure and function: Clinical implications. *Biological Psychiatry*, 48, 778–790.
- Kaufman, J., Yang, B., Douglas-Palumberi, H., Houshyar, S., Lipschitz, D., Krystal, J.H., et al. (2004). Social supports and serotonin transporter gene moderate depression in maltreated children. *Proceedings of the National Academy of Sciences of the United States of America*, 101, 17316–17321.
- Kauppi, A., Kumpulainen, K., Vanamo, T., Merikanto, J., & Karkola, K. (2008). Maternal depression and filicide-case study of ten mothers. *Archives of Women's Mental Health*, 11, 201–206.
- Keverne, E.B., & Curley, J.P. (2004). Vasopressin, oxytocin and social behaviour. *Current Opinion in Neurobiology*, 14, 777–783.
- Killgore, W.D.S., & Yurgelun-Todd, D.A. (2004). Activation of the amygdala and anterior cingulate during nonconscious processing of sad versus happy faces. *NeuroImage*, 21, 1215–1223.
- Kim, J., Kim, S., Kim, J., Jeong, B., Park, C., Son, A.R., et al. (2009a). Compassionate attitude towards others' suffering activates the mesolimbic neural system. *Neuropsychologia*, 47, 2073–2081.
- Kim, P., Leckman, J.F., Mayes, L.C., Newman, M., Feldman, R., & Swain, J.E. (2009b). Perceived quality of maternal care in childhood and structure and function of mothers' brain. *Developmental Science*, 13, 662–673.
- Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., et al. (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. *Journal of Neuroscience*, 25, 11489–11493.
- Klein, D.N., Arnow, B.A., Barkin, J.L., Dowling, F., Kocsis, J.H., Leon, A.C., et al. (2009). Early adversity in chronic depression: Clinical correlates and response to pharmacotherapy. *Depression and Anxiety*, 26, 701–710.
- Knutson, J.F. (1995). Psychological characteristics of maltreated children: Putative risk factors and consequences. *Annual Review of Psychology*, 46, 401–431.
- Koenigs, M., & Grafman, J. (2009). The functional neuroanatomy of depression: Distinct roles for ventromedial and dorsolateral prefrontal cortex. *Behavioural Brain Research*, 201, 239–243.
- Koo, V., Lynch, J., & Cooper, S. (2003). Risk of postnatal depression after emergency delivery. *Journal of Obstetrics and Gynaecology Research*, 29, 246–250.
- Kreppner, J.M., O'Connor, T.G., & Rutter, M. (2001). Can inattention/overactivity be an institutional deprivation syndrome? *Journal of Abnormal Child Psychology*, 29, 513–528.
- Kringelbach, M.L. (2005). The human orbitofrontal cortex: Linking reward to hedonic experience. *Nature Reviews. Neuroscience*, 6, 691–702.
- Krpan, K.M., Coombs, R., Zinga, D., Steiner, M., & Fleming, A.S. (2005). Experiential and hormonal correlates of maternal behavior in teen and adult mothers. *Hormones and Behavior*, 47, 112–122.
- Krumbholz, K., Nobis, E.A., Weatheritt, R.J., & Fink, G.R. (2009). Executive control of spatial attention shifts in the auditory compared to the visual modality. *Human Brain Mapping*, 30, 1457–1469.
- Laranjo, J., Bernier, A., & Meins, E. (2008). Associations between maternal mind-mindedness and infant attachment security: Investigating the mediating role of maternal sensitivity. *Infant Behavior and Development*, 31, 688–695.
- Leh, S.E., Petrides, M., & Strafella, A.P. (2010). The neural circuitry of executive functions in healthy subjects and Parkinson's disease. *Neuropsychopharmacology*, 35, 70–85.
- Leibenluft, E., Gobbini, M.I., Harrison, T., & Haxby, J.V. (2004). Mothers' neural activation in response to pictures of their children and other children. *Biological Psychiatry*, 56, 225–232.
- Leiderman, P., & Leiderman, M. (1977). Economic change and infant care in an East African agricultural community. In P.H. Leiderman, S.R. Tulkin, & A. Rosenfeld (Eds.), *Culture and infancy: Variations in human experience* (pp. 405–438). New York: Academic Press.
- Leifer, M. (1980). *Psychological effects of motherhood: A study of first pregnancy*. New York: Praeger.
- Levitan, R.D., Rector, N.A., Sheldon, T., & Goering, P. (2003). Childhood adversities associated with major depression and/or anxiety disorders in a community sample of Ontario: Issues of co-morbidity and specificity. *Depression and Anxiety*, 17, 34–42.
- Li, X., Lu, Z., D'Armenbeau, A., Ng, M., & Bechara, A. (2009). The Iowa Gambling Task in fMRI images. *Human Brain Mapping*, 31, 410–423.
- Lizardi, H., Klein, D.N., Ouimette, P.C., Riso, L.P., Anderson, R.L., & Donaldson, S.K. (1995). Reports of the childhood home environment in early-onset dysthymia and episodic major depression. *Journal of Abnormal Psychology*, 104, 132–139.
- Lorberbaum, J.P., Newman, J.D., Horwitz, A.R., Dubno, J.R., Lydiard, R.B., Hamner, M.B., et al. (2002). A potential role for thalamocingulate circuitry in human maternal behavior. *Biological Psychiatry*, 51, 431–445.
- Lovic, V., & Fleming, A.S. (2004). Artificially-reared female rats show reduced prepulse inhibition and deficits in the attentional set shifting task – reversal of effects with maternal-like licking stimulation. *Behavioural Brain Research*, 148, 209–219.
- Lovic, V., Gonzalez, A., & Fleming, A.S. (2001). Maternally separated rats show deficits in maternal care in adulthood. *Developmental Psychobiology*, 39, 19–33.
- Maestripietri, D. (2005). Early experience affects the intergenerational transmission of infant abuse in rhesus monkeys. *Proceedings of the National Academy of Sciences of the United States of America*, 102, 9726–9729.
- Marcus, S.M. (2009). Depression during pregnancy: Rates, risks and consequences – Motherisk Update 2008. *Canadian Journal of Clinical Pharmacology*, 16, e15–22.
- Martin, G., Bergen, H.A., Roeger, L., & Allison, S. (2004). Depression in young adolescents: Investigations using 2 and 3 factor versions of the Parental Bonding Instrument. *Journal of Nervous and Mental Disease*, 192, 650–657.
- Matsuo, K., Nicoletti, M., Nemoto, K., Hatch, J.P., Peluso, M.A.M., Nery, F.G., et al. (2009). A voxel-based morphometry study of frontal gray matter correlates of impulsivity. *Human Brain Mapping*, 30, 1188–1195.
- Mattson, B.J., & Morrell, J.I. (2005). Preference for cocaine- versus pup-associated cues differentially activates neurons expressing either Fos or cocaine- and amphetamine-regulated transcript in lactating, maternal rodents. *Neuroscience*, 135, 315–328.
- Mayberg, H.S., Lozano, A.M., Voon, V., McNeely, H.E., Seminowicz, D., Hamani, C., et al. (2005). Deep brain stimulation for treatment-resistant depression. *Neuron*, 45, 651–660.
- McCauley, J., Kern, D.E., Kolodner, K., Dill, L., Schroeder, A.F., DeChant, H.K., et al. (1997). Clinical characteris-

- tics of women with a history of childhood abuse: Unhealed wounds. *Journal of the American Medical Association*, 277, 1362–1368.
- McEwen, B.S. (2003). Early life influences on life-long patterns of behavior and health. *Mental Retardation and Developmental Disabilities Research Reviews*, 9, 149–154.
- Meins, E., Fernyhough, C., Fradley, E., & Tuckey, M. (2001). Rethinking maternal sensitivity: Mothers' comments on infants' mental processes predict security of attachment at 12 months. *Journal of Child Psychology and Psychiatry*, 42, 637–648.
- Meins, E., Fernyhough, C., Russell, J., & Clark-Carter, D. (1998). Security of attachment as a predictor of symbolic and mentalising abilities: A longitudinal study. *Social Development*, 7, 1–24.
- Meins, E., Fernyhough, C., Wainwright, R., Clark-Carter, D., Das Gupta, M., Fradley, E., et al. (2003). Pathways to understanding mind: Construct validity and predictive validity of maternal mind-mindedness. *Child Development*, 74, 1194–1211.
- Meins, E., Fernyhough, C., Wainwright, R., Das Gupta, M., Fradley, E., & Tuckey, M. (2002). Maternal mind-mindedness and attachment security as predictors of theory of mind understanding. *Child Development*, 73, 1715–1726.
- Melo, A.I., Lovic, V., Gonzalez, A., Madden, M., Sinopoli, K., & Fleming, A.S. (2006). Maternal and littermate deprivation disrupts maternal behavior and social-learning of food preference in adulthood: Tactile stimulation, nest odor, and social rearing prevent these effects. *Developmental Psychobiology*, 48, 209–219.
- Milad, M.R., & Rauch, S.L. (2007). The role of the orbitofrontal cortex in anxiety disorders. *Annals of the New York Academy of Sciences*, 1121, 546–561.
- Miller, L., Kramer, R., Warner, V., Wickramaratne, P., & Weissman, M. (1997). Intergenerational transmission of parental bonding among women. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36, 1134–1139.
- Miller, L., Warner, V., Wickramaratne, P., & Weissman, M. (1999). Self-esteem and depression: Ten year follow-up of mothers and offspring. *Journal of Affective Disorders*, 52, 41–49.
- Mitchell, J.P., Neil Macrae, C., & Banaji, M.R. (2005). Forming impressions of people versus inanimate objects: Social-cognitive processing in the medial prefrontal cortex. *NeuroImage*, 26, 251–257.
- Modirrousta, M., & Fellows, L.K. (2008). Dorsal medial prefrontal cortex plays a necessary role in rapid error prediction in humans. *Journal of Neuroscience*, 28, 14000–14005.
- Moehler, E., Biringen, Z., & Poustka, L. (2007). Emotional availability in a sample of mothers with a history of abuse. *American Journal of Orthopsychiatry*, 77, 624–628.
- Monchi, O., Petrides, M., Petre, V., Worsley, K., & Dagher, A. (2001). Wisconsin Card Sorting revisited: Distinct neural circuits participating in different stages of the task identified by event-related functional magnetic resonance imaging. *Journal of Neuroscience*, 21, 7733–7741.
- Moritz, S., Birkner, C., Kloss, M., Jahn, H., Hand, I., Haasen, C., & Krausz, M. (2002). Executive functioning in obsessive-compulsive disorder, unipolar depression, and schizophrenia. *Archives of Clinical Neuropsychology*, 17, 477–483.
- Moses-Kolko, E.L., & Roth, E.K. (2004). Antepartum and postpartum depression: Healthy mom, healthy baby. *Journal of the American Medical Women's Association*, 59, 181–191.
- Moskvina, V., Farmer, A., Swainson, V., O'Leary, J., Gunasinghe, C., Owen, M., et al. (2007). Interrelationship of childhood trauma, neuroticism, and depressive phenotype. *Depression and Anxiety*, 24, 163–168.
- Moss, H.A., & Jones, S.J. (1977). Relations between maternal attitudes and maternal behavior as a function of social class. In P.H. Leiderman, S.R. Tulkin, & A. Rosenfeld (Eds.), *Culture and infancy*. New York: Academic Press.
- Murray, L., Woolgar, M., Murray, J., & Cooper, P. (2003). Self-exclusion from health care in women at high risk for postpartum depression. *Journal of Public Health Medicine*, 25, 131–137.
- Nachmias, M., Gunnar, M., Mangelsdorf, S., Parritz, R.H., & Buss, K. (1996). Behavioral inhibition and stress reactivity: The moderating role of attachment security. *Child Development*, 67, 508–522.
- Nagahama, Y., Okada, T., Katsumi, Y., Hayashi, T., Yamauchi, H., Oyanagi, C., et al. (2001). Dissociable mechanisms of attentional control within the human prefrontal cortex. *Cerebral Cortex*, 11, 85–92.
- Nakano, Y., Baba, H., Maeshima, H., Kitajima, A., Sakai, Y., Baba, K., Suzuki, T., et al. (2008). Executive dysfunction in medicated, remitted state of major depression. *Journal of Affective Disorders*, 111, 46–51.
- Nee, D.E., & Jonides, J. (2009). Common and distinct neural correlates of perceptual and memorial selection. *NeuroImage*, 45, 963–975.
- Nelson, E.E., Herman, K.N., Barrett, C.E., Noble, P.L., Wojteczko, K., Chisholm, K., et al. (2009). Adverse rearing experiences enhance responding to both aversive and rewarding stimuli in juvenile rhesus monkeys. *Biological Psychiatry*, 66, 702–704.
- Nemeroff, C.B., Bissette, G., Akil, H., & Fink, M. (1991). Neuropeptide concentrations in the cerebrospinal fluid of depressed patients treated with electroconvulsive therapy. Corticotrophin-releasing factor, beta-endorphin and somatostatin. *British Journal of Psychiatry*, 158, 59–63.
- Nemeroff, C.B., Widerlöv, E., Bissette, G., Walléus, H., Karlsson, I., Eklund, K., et al. (1984). Elevated concentrations of CSF corticotropin-releasing factor-like immunoreactivity in depressed patients. *Science*, 226, 1342–1344.
- Nierop, A., Bratsikas, A., Zimmermann, R., & Ehlert, U. (2006). Are stress-induced cortisol changes during pregnancy associated with postpartum depressive symptoms? *Psychosomatic Medicine*, 68, 931–937.
- Nitschke, J.B., Nelson, E.E., Rusch, B.D., Fox, A.S., Oakes, T.R., & Davidson, R.J. (2004). Orbitofrontal cortex tracks positive mood in mothers viewing pictures of their newborn infants. *NeuroImage*, 21, 583–592.
- Nitschke, J. B., Sarinopoulos, I., Oathes, D. J., Johnstone, T., Whalen, P. J., Davidson, R. J., et al. (2009). Anticipatory activation in the amygdala and anterior cingulate in generalized anxiety disorder and prediction of treatment response. *American Journal of Psychiatry*, 166, 302–310.
- Nolin, P., & Ethier, L. (2007). Using neuropsychological profiles to classify neglected children with or without physical abuse. *Child Abuse and Neglect*, 31, 631–643.
- Noriuchi, M., Kikuchi, Y., & Senoo, A. (2008). The functional neuroanatomy of maternal love: Mother's response to infant's attachment behaviors. *Biological Psychiatry*, 63, 415–423.
- Numan, M. (2007). Motivational systems and the neural circuitry of maternal behavior in the rat. *Developmental Psychobiology*, 49, 12–21.

- Numan, M., Fleming, A.S., & Levy, F. (2006). Maternal behavior. In J.D. Neill (Ed.), *Knobil and Neill's physiology of reproduction* (pp. 1921–1993). San Diego, CA: Elsevier.
- Numan, M., & Insel, T. (2003). *The neurobiology of parental behavior*. New York: Springer.
- O'Hara, M.W., Zekoski, E.M., Philipps, L.H., & Wright, E.J. (1990). Controlled prospective study of postpartum mood disorders: Comparison of childbearing and non-childbearing women. *Journal of Abnormal Psychology*, 99, 3–15.
- Olazábal, D.E., Abercrombie, E., Rosenblatt, J.S., & Morrell, J.I. (2004). The content of dopamine, serotonin, and their metabolites in the neural circuit that mediates maternal behavior in juvenile and adult rats. *Brain Research Bulletin*, 63, 259–268.
- Palombo, D.J., Nowoslawski, M., & Fleming, A.S. (2010). Motherless rats show deficits in maternal behavior towards fostered pups. *Developmental Psychobiology*, 52, 142–148.
- Pak-Gorstein, S., Haq, A., & Graham, E.A. (2009). Cultural influences on infant feeding practices. *Pediatrics in Review*, 30, e11–21.
- Panthangi, V., West, P., Savoy-Moore, R.T., Geeta, M., & Reickert, E. (2009). Is seasonal variation another risk factor for postpartum depression? *Journal of the American Board of Family Medicine*, 22, 492–497.
- Paris, R., Bolton, R.E., & Weinberg, M.K. (2009). Postpartum depression, suicidality, and mother–infant interactions. *Archives of Women's Mental Health*, 12, 309–321.
- de Paül, J., & Domenech, L. (2000). Childhood history of abuse and child abuse potential in adolescent mothers: A longitudinal study. *Child Abuse and Neglect*, 24, 701–713.
- Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Reviews. Neuroscience*, 2, 417–424.
- Pears, K., & Fisher, P.A. (2005). Developmental, cognitive, and neuropsychological functioning in preschool-aged foster children: Associations with prior maltreatment and placement history. *Journal of Developmental and Behavioral Pediatrics*, 26, 112–122.
- Pears, K.C., Kim, H.K., & Fisher, P.A. (2008). Psychosocial and cognitive functioning of children with specific profiles of maltreatment. *Child Abuse and Neglect*, 32, 958–971.
- Pederson, D.R., Moran, G., Sitko, C., Campbell, K., Ghesquire, K., & Acton, H. (1990). Maternal sensitivity and the security of infant–mother attachment: A Q-sort study. *Child Development*, 61, 1974–1983.
- Penza, K.M., Heim, C., & Nemeroff, C.B. (2003). Neurobiological effects of childhood abuse: Implications for the pathophysiology of depression and anxiety. *Archives of Women's Mental Health*, 6, 15–22.
- Petrides, M. (2005). Lateral prefrontal cortex: Architectonic and functional organization. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 360, 781–795.
- Petrides, M., & Pandya, D.N. (1999). Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *European Journal of Neuroscience*, 11, 1011–1036.
- Pizzagalli, D.A., Holmes, A.J., Dillon, D.G., Goetz, E.L., Birk, J.L., Bogdan, R., et al. (2009). Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. *American Journal of Psychiatry*, 166, 702–710.
- Platak, S.M., & Kemp, S.M. (2009). Is family special to the brain? An event-related fMRI study of familiar, familial, and self-face recognition. *Neuropsychologia*, 47, 849–858.
- Pryce, C.R., Dettling, A., Spengler, M., Spaete, C., & Feldon, J. (2004). Evidence for altered monoamine activity and emotional and cognitive disturbance in marmoset monkeys exposed to early life stress. *Annals of the New York Academy of Sciences*, 1032, 245–249.
- Pryce, C.R., Martin, R.D., & Skuse, D. (1995). *Motherhood in human and nonhuman primates: Biosocial determinants*. New York: Karger.
- Putallaz, M., Costanzo, P.R., Grimes, C.L., & Sherman, D.M. (1998). Intergenerational continuities and their influences on children's social development. *Social Development*, 7, 389–427.
- Putnam, F.W. (2003). Ten-year research update review: Child sexual abuse. *Journal of the American Academy of Child and Adolescent Psychiatry*, 42, 269–278.
- Raes, F., Hermans, D., & Williams, J.M.G. (2006). Negative bias in the perception of others' facial emotional expressions in major depression: The role of depressive rumination. *Journal of Nervous and Mental Disease*, 194, 796–799.
- Ranote, S., Elliott, R., Abel, K.M., Mitchell, R., Deakin, J.F.W., & Appleby, L. (2004). The neural basis of maternal responsiveness to infants: An fMRI study. *Neuroreport*, 15, 1825–1829.
- Rao, U., Hammen, C., Ortiz, L.R., Chen, L., & Poland, R.E. (2008). Effects of early and recent adverse experiences on adrenal response to psychosocial stress in depressed adolescents. *Biological Psychiatry*, 64, 521–526.
- Rauch, S.L., Shin, L.M., & Phelps, E.A. (2006). Neurocircuitry models of posttraumatic stress disorder and extinction: Human neuroimaging research – past, present, and future. *Biological Psychiatry*, 60, 376–382.
- Ravizza, S.M., & Carter, C.S. (2008). Shifting set about task switching: Behavioral and neural evidence for distinct forms of cognitive flexibility. *Neuropsychologia*, 46, 2924–2935.
- Rebollo, A.G., & Montero, C.M. (2000). Variables perinatales y desigualdades en salud en un área sanitaria de Cáceres [Perinatal variables and health inequalities in a health-care district in Cáceres, Spain]. *Gaceta Sanitaria*, 14, 31–38.
- Rees, S.L., Akbari, E., Steiner, M., & Fleming, A.S. (2008). Effects of early deprivation and maternal separation on pup-directed behavior and HPA axis measures in the juvenile female rat. *Developmental Psychobiology*, 50, 315–321.
- Rees, S.L., Panesar, S., Steiner, M., & Fleming, A.S. (2004). The effects of adrenalectomy and corticosterone replacement on maternal behavior in the postpartum rat. *Hormones and Behavior*, 46, 411–419.
- Rees, S.L., Panesar, S., Steiner, M., & Fleming, A.S. (2006). The effects of adrenalectomy and corticosterone replacement on induction of maternal behavior in the virgin female rat. *Hormones and Behavior*, 49, 337–345.
- Repetti, R.L., Taylor, S.E., & Seeman, T.E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin*, 128, 330–366.
- Rey, J.M. (1995). Perceptions of poor maternal care are associated with adolescent depression. *Journal of Affective Disorders*, 34, 95–100.
- Righetti-Veltema, M., Conne-Perréard, E., Bousquet, A., & Manzano, J. (2002). Postpartum depression and mother–infant relationship at 3 months old. *Journal of Affective Disorders*, 70, 291–306.

- Rikhye, K., Tyrka, A.R., Kelly, M.M., Gagne, G.G., Mello, A.F., Mello, M.F., et al. (2008). Interplay between childhood maltreatment, parental bonding, and gender effects: Impact on quality of life. *Child Abuse and Neglect*, 32, 19–34.
- Risold, P.Y., Thompson, R.H., & Swanson, L.W. (1997). The structural organization of connections between hypothalamus and cerebral cortex. *Brain Research. Brain Research Reviews*, 24, 197–254.
- Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience*, 27, 169–192.
- Rizzolatti, G., & Fabbri-Destro, M. (2008). The mirror system and its role in social cognition. *Current Opinion in Neurobiology*, 18, 179–184.
- Roceri, M., Cirulli, F., Pessina, C., Peretto, P., Racagni, G., & Riva, M.A. (2004). Postnatal repeated maternal deprivation produces age-dependent changes of brain-derived neurotrophic factor expression in selected rat brain regions. *Biological Psychiatry*, 55, 708–714.
- Robson, K.S. (1967). The role of eye-to-eye contact in maternal-infant attachment. *Journal of Child Psychology and Psychiatry*, 87, 13–25.
- Robson, K.S., & Kumar, R. (1980). Delayed onset of maternal affection after childbirth. *British Journal of Psychiatry*, 136, 347–353.
- Rogers, M.A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K., et al. (2004). Executive and prefrontal dysfunction in unipolar depression: A review of neuropsychological and imaging evidence. *Neuroscience Research*, 50, 1–11.
- Rosenblatt, J.S. (1969). The development of maternal responsiveness in the rat. *American Journal of Orthopsychiatry*, 39, 36–56.
- Rosenblatt, J.S. (1975). Prepartum and postpartum regulation of maternal behaviour in the rat. *Ciba Foundation Symposium*, 33, 17–37.
- Rosenblatt, J.S., Olufowobi, A., & Siegel, H.I. (1998). Effects of pregnancy hormones on maternal responsiveness, responsiveness to estrogen stimulation of maternal behavior, and the lordosis response to estrogen stimulation. *Hormones and Behavior*, 33, 104–114.
- Rosenblum, L.A., Smith, E.L.P., Altemus, M., Scharf, B.A., Owens, M.J., Nemeroff, C.B., Gorman, J.M., et al. (2002). Differing concentrations of corticotrophin-releasing factor and oxytocin in the cerebrospinal fluid of bonnet and pigtail macaques. *Psychoneuroendocrinology*, 27, 651–660.
- Roth, T.L., Lubin, F.D., Funk, A.J., & Sweatt, J.D. (2009). Lasting epigenetic influence of early-life adversity on the BDNF gene. *Biological Psychiatry*, 65, 760–769.
- Rudorfer, M.V., Risby, E.D., Osman, O.T., Gold, P.W., & Potter, W.Z. (1991). Hypothalamic-pituitary-adrenal axis and monoamine transmitter activity in depression: A pilot study of central and peripheral effects of electroconvulsive therapy. *Biological Psychiatry*, 29, 253–264.
- Sarinopoulos, I., Grupe, D.W., Mackiewicz, K.L., Herrington, J.D., Lor, M., Steege, E.E., et al. (2009). Uncertainty during anticipation modulates neural responses to aversion in human insula and amygdala. *Cerebral Cortex*, 20, 929–940.
- Savitz, J.B., & Drevets, W.C. (2009). Imaging phenotypes of major depressive disorder: Genetic correlates. *Neuroscience*, 164, 300–330.
- Saxe, R., Moran, J.M., Scholz, J., & Gabrieli, J. (2006). Overlapping and non-overlapping brain regions for theory of mind and self reflection in individual subjects. *Social Cognitive and Affective Neuroscience*, 1, 229–234.
- Schoenbaum, G., Roesch, M.R., Stalnaker, T.A., & Takahashi, Y.K. (2009). A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. *Nature Reviews. Neuroscience*, 10, 885–892.
- Schorscher-Petcu, A., Dupré, A., & Tribollet, E. (2009). Distribution of vasopressin and oxytocin binding sites in the brain and upper spinal cord of the common marmoset. *Neuroscience Letters*, 461, 217–222.
- Schulte-Rüther, M., Markowitsch, H.J., Fink, G.R., & Piefke, M. (2007). Mirror neuron and theory of mind mechanisms involved in face-to-face interactions: A functional magnetic resonance imaging approach to empathy. *Journal of Cognitive Neuroscience*, 19, 1354–1372.
- Schulz, K.P., Clerkin, S.M., Halperin, J.M., Newcorn, J.H., Tang, C.Y., & Fan, J. (2009). Dissociable neural effects of stimulus valence and preceding context during the inhibition of responses to emotional faces. *Human Brain Mapping*, 30, 2821–2833.
- Seeman, T.E., Singer, B.H., Ryff, C.D., Dienberg Love, G., & Levy-Storms, L. (2002). Social relationships, gender, and allostatic load across two age cohorts. *Psychosomatic Medicine*, 64, 395–406.
- Seifritz, E., Esposito, F., Neuhoff, J.G., Lüthi, A., Mustovic, H., Dammann, G., et al. (2003). Differential sex-independent amygdala response to infant crying and laughing in parents versus nonparents. *Biological Psychiatry*, 54, 1367–1375.
- Serbin, L.A., & Karp, J. (2004). The intergenerational transfer of psychosocial risk: Mediators of vulnerability and resilience. *Annual Review of Psychology*, 55, 333–363.
- Sergerie, K., Chochol, C., & Armony, J.L. (2008). The role of the amygdala in emotional processing: A quantitative meta-analysis of functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews*, 32, 811–830.
- Sewards, T.V., & Sewards, M.A. (2002). Fear and power-dominance drive motivation: Neural representations and pathways mediating sensory and mnemonic inputs, and outputs to premotor structures. *Neuroscience and Biobehavioral Reviews*, 26, 553–579.
- Sewards, T.V., & Sewards, M.A. (2003). Representations of motivational drives in mesial cortex, medial thalamus, hypothalamus and midbrain. *Brain Research Bulletin*, 61, 25–49.
- Sheline, Y.I., Barch, D.M., Price, J.L., Rundle, M.M., Vaishnavi, S.N., Snyder, A.Z., et al. (2009). The default mode network and self-referential processes in depression. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 1942–1947.
- Shin, L.M., Rauch, S.L., & Pitman, R.K. (2006). Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. *Annals of the New York Academy of Sciences*, 1071, 67–79.
- Siegle, G. J., Thompson, W., Carter, C.S., Steinhauer, S.R., & Thase, M.E. (2007). Increased amygdala and decreased dorsolateral prefrontal BOLD responses in unipolar depression: Related and independent features. *Biological Psychiatry*, 61, 198–209.
- Simon, J.J., Walther, S., Fiebach, C.J., Friederich, H., Stippich, C., Weisbrod, M., et al. (2010). Neural reward processing is modulated by approach- and avoidance-related personality traits. *NeuroImage*, 49, 1868–1874.
- Smeltzer, M.D., Curtis, J.T., Aragona, B.J., & Wang, Z. (2006). Dopamine, oxytocin, and vasopressin receptor binding in the medial prefrontal cortex of monogamous and promiscuous voles. *Neuroscience Letters*, 394, 146–151.

- Smoski, M.J., Felder, J., Bizzell, J., Green, S.R., Ernst, M., Lynch, T.R., et al. (2009). fMRI of alterations in reward selection, anticipation, and feedback in major depressive disorder. *Journal of Affective Disorders*, 118(1–3), 69–78.
- Spertus, I.L., Yehuda, R., Wong, C.M., Halligan, S., & Seremetis, S.V. (2003). Childhood emotional abuse and neglect as predictors of psychological and physical symptoms in women presenting to a primary care practice. *Child Abuse and Neglect*, 27, 1247–1258.
- Spreng, R.N., & Grady, C.L. (2010). Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. *Journal of Cognitive Neuroscience*, 22, 1112–1123.
- Stallings, J., Fleming, A.S., Corter, C., Worthman, C., & Steiner, M. (2001). The effects of infant cries and odors on sympathy, cortisol, and autonomic responses in new mothers and nonpostpartum women. *Parenting: Science and Practice*, 1, 71–100.
- Strathearn, L., Fonagy, P., Amico, J., & Montague, P.R. (2009). Adult attachment predicts maternal brain and oxytocin response to infant cues. *Neuropsychopharmacology*, 34, 2655–2666.
- Strathearn, L., Li, J., Fonagy, P., & Montague, P.R. (2008). What's in a smile? Maternal brain responses to infant facial cues. *Pediatrics*, 122, 40–51.
- Swain, J.E. (2008). Baby stimuli and the parent brain: Functional neuroimaging of the neural substrates of parent–infant attachment. *Psychiatry*, 5, 28–36.
- Swain, J.E., Lorberbaum, J.P., Kose, S., & Strathearn, L. (2007). Brain basis of early parent–infant interactions: Psychology, physiology, and in vivo functional neuroimaging studies. *Journal of Child Psychology and Psychiatry*, 48, 262–287.
- Swain, J.E., Tasgin, E., Mayes, L.C., Feldman, R., Constable, R.T., & Leckman, J.F. (2008). Maternal brain response to own baby-cry is affected by cesarean section delivery. *Journal of Child Psychology and Psychiatry*, 49, 1042–1052.
- Swain, J.E., & Lorberbaum, J.P. (2008). Imaging the human parental brain. *Neurobiology of the parental brain* (pp. 83–100). Burlington, MA: Academic Press.
- Sweeney, J.A., Kmiec, J.A., & Kupfer, D.J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry*, 48, 674–684.
- Tamis-LeMonda, C.S., & Bornstein, M.H. (1989). Habituation and maternal encouragement of attention in infancy as predictors of toddler language, play, and representational competence. *Child Development*, 60, 738–751.
- Tamis-LeMonda, C.S., Bornstein, M.H., & Baumwell, L. (2001). Maternal responsiveness and children's achievement of language milestones. *Child Development*, 72, 748–767.
- Thoman, E.B. (2006). Co-sleeping, an ancient practice: Issues of the past and present, and possibilities for the future. *Sleep Medicine Reviews*, 10, 407–417.
- Thulier, D. (2009). Breastfeeding in America: A history of influencing factors. *Journal of Human Lactation*, 25, 85–94.
- Trehub, S., Unyk, A., & Trainor, L.J. (1993). Maternal singing in cross-cultural perspective. *Infant Behavior and Development*, 16, 285–295.
- Trevathan, W.R. (1983). Maternal 'en face' orientation during the first hours after birth. *American Journal of Orthopsychiatry*, 53, 92–99.
- van IJzendoorn, M.H. (1992). Intergenerational transmission of parenting: A review of studies in nonclinical populations. *Developmental Review*, 12, 76–99.
- van Sleuwen, B.E., Engelberts, A.C., Boere-Boonekamp, M.M., Kuis, W., Schulpen, T.W.J., & L'Hoir, M.P. (2007). Swaddling: A systematic review. *Pediatrics*, 120(4), e1097–1106. doi: 10.1542/peds.2006-2083.
- van Veen, V., & Carter, C.S. (2002). The anterior cingulate as a conflict monitor: fMRI and ERP studies. *Physiology and Behavior*, 77, 477–482.
- Vik, T., Grote, V., Escibano, J., Socha, J., Verduci, E., Fritsch, M., et al. (2009). Infantile colic, prolonged crying and maternal postnatal depression. *Acta Paediatrica*, 98, 1344–1348.
- Vogt, B.A., Nimchinsky, E.A., Vogt, L.J., & Hof, P.R. (1995). Human cingulate cortex: Surface features, flat maps, and cytoarchitecture. *Journal of Comparative Neurology*, 359, 490–506.
- Vogt, B.A., Vogt, L., Farber, N.B., & Bush, G. (2005). Architecture and neurocytology of monkey cingulate gyrus. *Journal of Comparative Neurology*, 485, 218–239.
- Wang, C., Ulbert, I., Schomer, D.L., Marinkovic, K., & Halgren, E. (2005). Responses of human anterior cingulate cortex microdomains to error detection, conflict monitoring, stimulus-response mapping, familiarity, and orienting. *Journal of Neuroscience*, 25, 604–613.
- Williams, M.A., McGlone, F., Abbott, D.F., & Mattingley, J.B. (2005). Differential amygdala responses to happy and fearful facial expressions depend on selective attention. *NeuroImage*, 24, 417–425.
- Willinger, U., Diendorfer-Radner, G., Willnauer, R., Jörgl, G., & Hager, V. (2005). Parenting stress and parental bonding. *Behavioral Medicine*, 31, 63–69.
- Wind, T.W., & Silvern, L. (1994). Parenting and family stress as mediators of the long-term effects of child abuse. *Child Abuse and Neglect*, 18, 439–453.
- Winstanley, C.A., Theobald, D.E.H., Cardinal, R.N., & Robbins, T.W. (2004). Contrasting roles of basolateral amygdala and orbitofrontal cortex in impulsive choice. *Journal of Neuroscience*, 24, 4718–4722.
- Wise, R.A. (2000). Interactions between medial prefrontal cortex and meso-limbic components of brain reward circuitry. *Progress in Brain Research*, 126, 255–262.
- Xie, R., He, G., Koszycki, D., Walker, M., & Wen, S.W. (2009). Fetal sex, social support, and postpartum depression. *Canadian Journal of Psychiatry*, 54, 750–756.
- Zahn, R., de Oliveira-Souza, R., Bramati, I., Garrido, G., & Moll, J. (2009). Subgenual cingulate activity reflects individual differences in empathic concern. *Neuroscience Letters*, 457, 107–110.

Accepted for publication: 22 June 2010

Published online: 1 October 2010