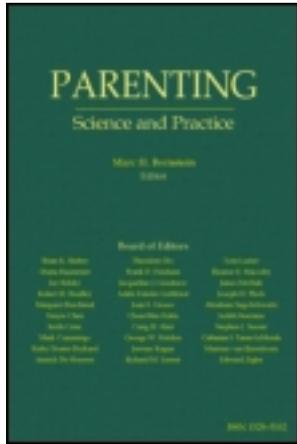


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Brain and Behavioral Modifications That Accompany the Onset of Motherhood

Kelly G. Lambert^a & Craig H. Kinsley^b

^a Department of Psychology, Randolph-Macon College, Ashland, VA, 23005, USA

^b University of Richmond

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Brain and Behavioral Modifications That Accompany the Onset of Motherhood

Kelly G. Lambert and Craig H. Kinsley

SYNOPSIS

Objective. To discuss the brain and behavioral modifications that accompany the onset of motherhood. **Design.** Following a consideration of the evolutionary significance of the emergence of nurturing and caring responses in mammals, a thorough analysis of neurobiological modifications thought to maintain maternal responses in both rodent models and humans is presented. **Results.** The dramatic neurobiological changes accompanying the onset of parental responses provide a unique model for investigating the dynamic nature of the brain in response to changing demands. **Conclusions.** As conveyed throughout this tutorial, the maternal brain is a striking example of the adaptation necessary for various aspects of mammalian survival.

INTRODUCTION

Previously only responsible for her own physiological needs and functions, a new rodent mother faces the appearance of approximately a dozen helpless pups, which demands the immediate emergence of a novel response repertoire. The new mother must groom her pups on delivery (Figure 1); keep them grouped in a writhing huddle to facilitate thermoregulation when she is not near; adapt a new humpbacked posture to allow the pups to nurse without being crushed by her body weight; and, because she is now engaged in metabolically costly lactation, she must forage for food in the most efficient manner possible, expending minimal energy for maximal calories. To avoid losing her vulnerable pups to predation, the maternal rodent must return to the nest quickly after foraging; and, last, she must be bold in her attempts to defend and/or protect her pups in the presence of a host of environmental threats. Such a demanding set of new job descriptions requires the rapid development of significant neurobiological modifications. The stakes are high: Failure to adapt to these new demands results in the loss of the mother's metabolic and valuable genetic investment.

Because humans and rodents share the same neural structures and chemicals, rodent models serve as a valuable tool for thorough investigations of the maternal brain. Although caution should be taken when generalizing across species, investigations of the neurobiological mechanisms accompanying the transformation from the virgin to the maternal brain may provide important clues about the evolution of the mammalian brain, especially the emergence of social and nurturing responses. Concomitant modifications in the maternal brain directed toward enhancing the survival of another animal, for example, represents a dramatic shift from the minimal maternal investment observed in reptilian species. MacLean (1990) considered the evolutionary significance of the emergence of the mammalian maternal response in *The Triune Brain in*



FIGURE 1
A maternal rat grooms her offspring.

Evolution. According to MacLean (1990), three behaviors distinguished mammals from their nonmammalian counterparts: nursing, mother-infant audio-vocal communications, and play behavior. Because these responses are related to maternal behavior and early social interactions among the pups occurring in the presence of the mother, the emergence of maternal care in evolutionarily early mammals may have guided the evolutionary trajectory toward more complex responses such as language, nurturing, and empathic responses.

This tutorial is an illumination of neurobiological (e.g., neuroanatomical, neurochemical, and neurophysiological) and behavioral changes that accompany the transition into motherhood. Because most of the work in this area has been conducted using rodents, we focus on research using these well-established models; relevant human work, however, is considered when appropriate. The rodent models, admittedly simpler than the human parental model, should not be deemed too foreign to facilitate understanding the framework for parenting in humans. Throughout this article we discuss the value of the parental model for a more general exemplar of neuroplasticity. The presence of offspring triggers the emergence of dramatic neurobiological events in maternal brains, providing neuroscientists with a solid model of the brain's natural ability to adapt to changing physiological and environmental demands, thereby assuring the survival of offspring, their significant genetic investment, and legacy.

BUILDING A BRAIN FOR MATERNAL BEHAVIOR

It can be argued that mothers are made, not born (see Bridges, 2008; Gonzalez-Mariscal & Kinsley, 2009; Kinsley et al., 2008; Kinsley & Lambert, 2006, 2008; Lambert & Kinsley, 2008). The requisite processes involve a cocktail of hormones, neuropeptides, and neurotransmitters, including prolactin, estrogen/estradiol, progesterone, dopamine, oxytocin and, surprisingly, the stress hormone cortisol as well as a host of neural regions that are modified through interactions with this neurochemical environment. Together, the neurochemical and neuroanatomical adaptations ensure adequate maternal care and successful reproduction for mammalian species, with only rare exceptions leading to dysfunctional maternal care.

Maternal behavior in the rodent—broadly defined and involving interlocking motivational, sensory, and motor components—involves a multitude of new offspring-directed behaviors in addition to significant modifications of existing responses (Bridges, 2008; Gubernick, 1981; Numan & Insel, 2003; Wiesner & Sheard, 1933). For instance, well before pups appear, the pending mother's metabolic requirements ascend precipitously as she must obtain more provisions for herself and the forthcoming litter, which is particularly protein keen. She begins to construct and provision a more elaborate nest in preparation for the collection of her vulnerable and temporarily thermally incapable offspring. All of these behaviors require regulation by different brain regions at different times, and eventually their seamless integration, balanced against environmental exigencies that may change second to second, requiring rapid behavioral adjustments on the part of the mother. The mother must be capable of distinguishing her young and friendly/unfriendly conspecifics and be capable of defending her nest and her young from predators or rogue males and females. She must hunt, eat, drink, and sleep in a different pattern from before; forage more efficiently; and remember the location of food and water caches and potential danger spots. In short, there is a marked difference between what she knew (or had to know) before her pups were born, and what she is required to learn and remember to care for offspring: She must learn, figuratively and literally, to think on the run. In essence, she has the added responsibilities for pup care on top of her already strenuous demands for personal survival. In response to these new demands, improvements to the mother's cognitive and stress-mediation apparatuses have been observed in maternal rats facilitating her management of the burdens of motherhood.

Virgin female and male rats will not readily exhibit parental responses, suggesting that the changes that accompany the reproductive experience ultimately prime the brain to respond to a new and unique set of stimuli (*viz.*, the pups). That is, there is an inherent responsiveness in females, expressed during the course of pregnancy (through exposure to the hormones of pregnancy), culminating in the full repertoire of maternal behaviors. In contrast, the male rat does not naturally care for offspring, often displaying infanticidal responses toward pups (Numan & Insel, 2003). A focus of parental animal models has been the illumination of brain areas critical for facilitating the adaptive interpretation of relevant sensory and motor cues as well as the requisite motivation and sustained responsiveness toward the pups. Functional magnetic resonance imaging studies in human parents are beginning to confirm many of the areas described in the animal work and extend to additional areas that may be involved with emotions such as empathy that would be expected to increase in response to young in human parents (Barrett & Fleming, 2011; Kim et al., 2010; Macbeth & Luine, 2010; Swain, 2011).

In rodents, lesions of the cingulate cortex and associated areas have been found to impair maternal retrieval behavior, possibly because of a decreased responsiveness to infant crying, a response critical for the maintenance of mother-offspring contact (Murphy, MacLean, & Hamilton, 1981; MacLean, 1990; Slotnick & Nigrosh, 1975; Stamm, 1955; MacLean & Newman, 1988). Lorberbaum and colleagues (1999) were among the first to examine the brain basis of human maternal behavior, by having mothers listen to recorded infant cries and white noise control sounds while they underwent functional magnetic resonance imaging of their brains. The anterior cingulate and right medial prefrontal cortex, brain areas associated with emotional regulation, planning, and decision making, showed statistically significantly increased activity with the cries compared with the control sounds, demonstrating that the anterior cingulate may be

involved in mothers listening/responding to babies that are in distress. Past research conducted by Swain and colleagues (Swain, 2008; Swain & Lorberbaum, 2008; Swain, Lorberbaum, Kose, & Strathearn, 2007) also demonstrated substantial activation in brain regions regulating emotion in the brains of parents. More recently, this team tracked gray matter changes either 2–4 weeks or 3–4 months postpartum and found increases in the midbrain areas, parietal lobes, and prefrontal cortex. Implicating the essential role of emotions in maternal responsiveness, the mothers possessing a more positive perception of her baby experienced greater gray matter volume changes (Kim et al., 2010). Thus, a parent, whether rat or human, becomes a parent through changes in the brain's morphology and activity. Lorberbaum (1999, p. 99) stated that further research on the maternal brain

may help (1) unravel the functional neuroanatomy of the parent-infant bond and (2) examine whether markers of this bond, such as maternal brain response to infant crying, can predict maternal style (i.e., child neglect), offspring temperament, or offspring depression or anxiety.

In the rat, neural areas associated with spatial memory appear to improve following reproductive experience (Kinsley et al., 1999). In two different spatial tasks (an eight-arm radial maze and a dry land maze [a Morris water maze analog that requires the animal to remember the location of a previously baited food well; Kesner & Dakis, 1995]), albino Sprague-Dawley and hooded Long-Evans parous female strains of rats were significantly faster at remembering the location of preferred food rewards (Pawluski, Vanderbyl, Ragan, & Galea, 2006; Pawluski, Walker, & Galea, 2006). Bodensteiner, Cain, Ray, and Hamula (2006) reported no effect during pregnancy, but subsequent enhancements occur, again favoring reference memory in rodents. Lambert and colleagues (2005) reported that offspring play a significant (and likely enriching) role in maternal memory enhancements. Pup-sensitized nulliparous females were significantly better in the dry land maze than were virgins and nearly as good as lactating females with pups (Kinsley et al., 1999). The enhanced spatial memory effect persists well into senescence (24+ months) in the female rat, with multiparous females showing the greatest effects on behavior (maze learning and memory) and brain (generally healthier looking, with fewer hippocampal deposits of the deleterious substance, amyloid precursor protein; Gatewood et al., 2005). There are also significant alterations of hippocampal neuronal microarchitecture, in particular increased dendritic spine concentrations in the Cornu Ammonis (CA1) area (known for its involvement with spatial memory and memory in rodents), which are increased in late-pregnant, lactating, and pregnancy hormone-treated females (Kinsley et al., 2006).

The data for postpartum human females demonstrated by Kim et al. (2010) and others raise questions regarding the brain's reactions to the interplay between mother and baby, and the receipt of cues from the offspring, that rich exchange of mother-child attention that virtually defines early parenthood. Lenzi et al. (2009) reported that healthy human mothers with infants less than 1 year old used a specific right hemisphere neural circuit, comprising the mirror neuron system (defined as the ventral premotor cortex, posterior parietal cortex, and inferior frontal gyrus), the insula, and amygdala, when they were interpreting and imitating emotional, rather than neutral, pictures of their infants. The authors emphasized the importance of the activation of this empathy system when infants are preverbal, requiring the mothers to share emotions with the infants and understand their needs.

The sum of such changes and improvements would likely contribute to spending less time away from the nest and, overall, the creation of a more secure nest. Furthermore, as intimated by Kim et al. (2010), the potent steroidal cocktail characteristic of pregnancy (estrogen, progesterone, prolactin, cortisol), followed by the intricate array of the babies' multisensorial inputs to their mother's brains, may produce the manifest alterations leading to the inherent neuroplasticity of the maternal brain. In addition, such research provides clues about where to look when the mother in question is perhaps indifferent to or lacking in adequate feeling for the infant (Barrett & Fleming, 2011). The mélange of sights, smells, sounds, suckling stimulation, and somatosensorial cues from young may have a significant effect on the way the maternal brain unfolds and dictates the consequent behaviors.

HORMONE-CELLULAR UNDERPINNINGS OF THE MATERNAL BRAIN

To be sure, a significant amount of neural restructuring is occurring as the animal transitions from self-directed virgin to other-directed new mother. At first, maternal behavior consists of a suite of several readily observed and hormonally stimulated behaviors that become stronger and experimentally observable with advancing pregnancy (Rosenblatt, 1975; Rosenblatt, Mayer, & Giordano, 1988; Terkel & Rosenblatt, 1968). A second phase, postpartum maternal behavior, is likewise heavily under hormonal control; for instance, estradiol, prolactin, and oxytocin (Brunton & Russell, 2008; Cameron et al., 2008; Moltz, Lubin, Leon, & Numan, 1970; Orpen, Furman, Wong, & Fleming, 1987; Pedersen, Vadlamudi, Boccia, & Amico, 2006; Rosenblatt, Olufowobi, & Siegel, 1998). These hormones interact to produce and preserve a responsive neural substrate, on which pup stimuli subsequently are capable of acting. Whereas hormonal exposure during pregnancy is requisite for full maternal behavior, exposure to pups or pup cues alone can induce maternal behavior and a significant preference for pups in virgin females (Fleming & Rosenblatt, 1974; Seip & Morrell, 2008; Svare & Gandelman, 1976). Such stimuli may also produce modifications in ancillary brain regions involved in supporting maternal behaviors (see Kinsley et al., 1999; Lambert et al., 2005). Lactating females require pup contact (or at least pup cues/exposure) to fully display maternal behavior and maternal supporting behaviors (*viz.*, postpartum aggression; Svare & Gandelman, 1976). Thus, mounting evidence suggests that internal (hormonal) and external (sensory stimuli from pups) environments coalesce to induce maternal behavior and offspring care in the new mother.

The development of maternal responsiveness through hormonal modifications may result in long-term neuronal changes (Gatewood et al., 2005; Kinsley, 1994; Kinsley & Bridges, 1988, 1990; Kinsley et al., 2008; Love et al., 2005). For example, it was demonstrated that the medial preoptic area (mPOA), an anterior hypothalamic structure, plays a major role in the regulation of maternal behavior. The mPOA possesses a high concentration of estradiol and progesterone receptors and must be intact (*i.e.*, not lesioned or malfunctioning) for maternal behavior to occur (Fahrbach & Pfaff, 1986; Numan, 1974; Numan & Insel, 2003; Numan, Rosenblatt, & Komisaruk, 1977). Gubernick, Sengelau, and Kurz (1993) reported that mPOA neuron somal size increased in females after pregnancy, parturition, and the initiation of maternal behavior. This reported effect in mPOA neurons in the female rat following a pregnancy pattern and maternal behavior-stimulating hormonal regimen suggests strongly that hormonal stimulation of

neurons in specific areas of the brain—in this case, an area known to regulate the overall expression of maternal behavior—results in behavior-relevant alterations. Steroid hormones estradiol and progesterone, the reproductive hormones manipulated in this experimental work, play major roles in these effects.

What of the molecular interface between hormone and neuron? Neurons easily bind steroid hormones via intracellular and membrane receptor sites, thereby modifying the genomic expression of proteins and, ultimately, the structure, wiring patterns, and activity of the neuron or groups of neurons (Levitan & Kaczmarek, 1991; McEwen, 1991; Woolley, Gould, Frankfurt, & McEwen, 1990). In the adult, as the neurons in a nucleus or neural circuit are activated, behaviors under the mediation of gonadal steroids such as sexual and maternal responses are themselves activated or modified. In addition to altering neurobiological activity, do hormones induce obvious changes in the structure of the adult neuron? Numerous studies have reported that estradiol and progesterone modify the structure of the neuron in the adult female brain, particularly dendritic spines (Brusco et al., 2008; Keyser-Marcus et al., 2001; Kinsley et al., 2006; McEwen & Woolley, 1994; Woolley et al., 1990; Woolley & McEwen, 1993). The latter effects occur with relatively short exposure to the hormones, primarily estradiol. Progesterone has a biphasic effect, in that progesterone exposure following estradiol initially increases spine density (sites that allow for additional synaptic inputs; Kuno, 1995; Levitan & Kaczmarek, 1991), but then stimulates a regression of spines greater in magnitude than with estradiol alone (Woolley & McEwen, 1993). If the level or pattern of estradiol and progesterone was altered or increased—as occurs during pregnancy—there may be even greater effects on the morphology of the neuron. Research has indicated that females from groups exposed to such hormonal treatments display significant increases in dendritic spine density in hippocampal CA1 neurons; Kinsley et al., 2006; see Figure 2 for comparison of dendritic spines in virgin and primiparous-like females).

Investigations into the structure and subsequent function of the maternal brain are beginning to show many striking effects that complement and reach beyond the anterior hypothalamus/mPOA. In addition to the data on morphology of neurons in the hippocampus (Brusco et al., 2008; Kinsley et al., 2006; Pawluski & Galea, 2005), others (Rasia-Filho, Fabian, Rigoti, & Achaval, 2004) have identified pregnancy hormonal effects in the amygdala (a component of the limbic system known for its involvement in fear responses). These data suggest a wide-ranging maternal circuitry in service to successful reproduction. Hormonal activation of mPOA neurons may increase and

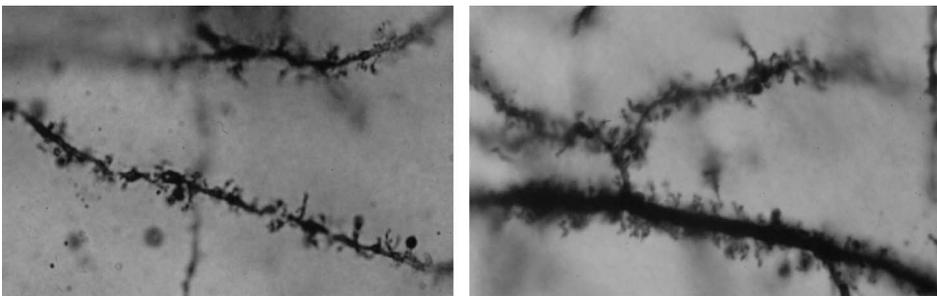


FIGURE 2

Hippocampal neurons (from the CA1 region) in virgin female rat (*left*) and similar neurons in lactating female rat (*right*). The short extensions of the dendrite, known as *spines*, increase the potential neural synaptic points in the nervous system.

modify the processing of information relevant for the exhibition of maternal behavior. For example, Numan and Numan (1995) reported that maternal behavior is accompanied by neural c-Fos (a proto oncogene denoting cellular activation) expression in mPOA, an effect reduced by morphine, which inhibits maternal behavior (Bridges & Grimm, 1982; Kinsley & Bridges, 1990). Perhaps mPOA neurons exposed to considerable amounts of steroid hormones throughout pregnancy alter their ability to respond to the heightened afferent sensory input that will be present on delivery of the pups, a set of stimulatory cues and signaling objects that require maternal attention. Steroid hormones have the capacity to modify membrane potentials, electrical activity, and interactions inherent to neurons in the hypothalamus (Joels, Heslen, Karst, & de Kloet, 1994; McEwen, 1991; Pfaff, 1989). Many hormones (prominently estradiol) can alter the resting and response firing rates of neurons in the hypothalamus (Pfaff, 1981) and apoptosis in the hippocampus (Liu et al., 2001). The circuitry into which such neurons are inserted would be expected to differ considerably from their prepregnancy state. Add changes that occur in neurochemistry in the brains of pregnant/parous females (e.g., many changes in neuropeptides, opioids, neurotransmitters), and a neuron from a pregnant or lactating female—from many different neuroanatomical sites—may be substantially different in form and function from one taken from a virgin female (Bridges, Felicio, Pellerin, Stuer, & Mann, 1993; Keverne & Kendrick, 1990; Kinsley & Bridges, 1988; Mann & Bridges, 1992).

Striking anatomical alterations occur in the brain awash in the hormones of pregnancy. Estradiol and progesterone stimulate the proliferation (and subsequent regression) of hippocampal dendritic spines (Woolley & McEwen, 1993) and generally increase the surface area of the neuron. If gonadal steroids affect neuronal size or activity in mPOA, and if such short-term hormonal exposure can dramatically affect neuronal structure, it is not surprising to discover (potentially long-lasting) alterations of hippocampal neuron structure in females exposed to the hormones of pregnancy.

Therefore, an interesting picture is beginning to emerge regarding (mainly) gonadal steroid regulation of brain regions involved in the initiation of maternal behavior as well as those playing a vital, but subordinate, role. For instance, hormone-induced modifications in hippocampus may facilitate requisite navigation skills involved in resource-gathering behaviors in which the female is engaged, which would facilitate the mother's departure from and more rapid return to the nest. Changes in the volume of the hippocampus (in this particular case, in males during the breeding season) correlate with changes in home range size, which suggests an environmentally responsive neural substrate with obvious behavioral ramifications: a male that can range farther and wider in search of mates (Jacobs, Gaulin, Sherry, & Hoffman, 1990). Therefore, concurrent alterations in the hippocampus and the mPOA may contribute to the marked behavioral transition characteristic of the maternal female, with one site (mPOA) concerned with maternal behavior the other (the hippocampus) with support behaviors (foraging). In sum, the ramping-up of neural activity is considerable and focused. Together, these modifications represent neuroplastic and behavioral changes accompanying the maternal experience.

NEUROBIOLOGICAL MODIFICATIONS FACILITATE ANCILLARY MATERNAL RESPONSES

Being a successful mammalian mother requires modifications in behaviors beyond the nest. That is, maternal behavior is only half the game. More efficient foraging strategies

and enhanced boldness appear to be important additions to the successful mother's behavioral repertoire. In the past, males have been unreliable parental partners. Hence, in a sense, the rat model is a working single mother model in that the female rat must provide all the resources for raising healthy offspring including food for the pups, food for herself, shelter, and an adequate nest located in appropriate habitat.

One of the earliest attempts to demonstrate modifications in behaviors beyond the nest assessed maternal and virgin rats in two spatial memory tasks: the dry land maze and the radial arm maze. In both tasks, different species of rats with maternal experience acquired the task and exhibited fewer errors than their virgin counterparts. In the dry land maze spatial task, females with past exposure to pups (i.e., foster or adoptive dams) joined the maternal animals in performing the tasks more efficiently than virgin rats, and almost as well as the lactating group (Kinsley et al., 1999). These results provided strong evidence that the maternal experience (pregnancy plus pup exposure and just pup exposure) dramatically altered the foraging strategies of the female rat.

Exploring further interactions between the roles of pregnancy and pup exposure, another study explored the contributions of pregnancy and pup exposure separately and in isolation by assessing cognitive strategies in virgins with and without pup exposure and maternal rats that were either allowed to lactate or were removed from the pups. In the probe trial of the maze administered at the end of the training period, a trial in which there was no food reward, the animals' problem-solving abilities were assessed when the rules of the game (i.e., Froot Loop reward in a consistent well) were altered. In essence, the probe trial allows the experimenters to determine where the rat goes when the expected well is no longer baited. In general, animals with enhanced memory spend more time in proximity to the previously baited well which is interpreted as a stronger memory for the task. The fully maternal animals in this trial spent more time in proximity to the previously baited well than the other groups and visited more of the wells that had been baited during the habituation phase of the study. Hence, the maternal animals appeared to maximize the probability of finding food by returning to the most likely source for the food and visiting other possible sources when no food was found. These behavioral changes occurred in animals that had delivered their pups 10 days earlier, suggesting that these foraging strategies and accompanying underlying brain changes may be long-lasting (Lambert et al., 2005).

Subsequent research confirmed that these modifications could be extended to more general learning tasks. In pregnant rats, enhancements in spatial working memory, assessed in the Morris water maze, were observed following about a week of pregnancy (Galea et al., 2000). This task, requiring the animals to remember the location of a submerged platform in a circular pool, also assesses spatial memory but in the context of an escape task because swimming is considered a significant stressor for rats. In another learning task, the object placement task, the animal is exposed to two novel objects followed by an inter-trial interval of a couple of hours followed by exposure to the same objects but with one moved to a new area of the enclosure. Pregnant rats spent more time investigating the novel object location, a behavior indicative of better spatial ability/memory because it appears that the animal remembers exploring the other object in the familiar placement, whereas the nonpregnant rats divided their time equally between the objects (Macbeth, Gautreaux, & Luine, 2008; Macbeth & Luine, 2010).

Focusing more specifically on the postpartum period, a time in which altered behavioral strategies are more critical due to the presence of the pups, further modifications

in seemingly adaptive responses have been observed. Using the attention set-shifting paradigm (Birrell & Brown, 2000), a task designed to assess rats' ability to shift their attention toward the most salient cues predicting the presence of food, virgins, first-time maternal rats, and second-time maternal rats were assessed. In particular, rats were trained to dig for Froot Loop rewards in small flower pots containing the same bedding medium but different odors, only one of which was associated with the presence of the food reward. In increasingly difficult phases of this task, the rats were required to ignore distracting cues such as new odors and bedding media and focus on the most salient cues. In the most difficult phases of the task, the previous distracting cue of bedding type becomes the salient cue requiring the rats to alter their response strategies based on changing payoffs, while ignoring previously reinforced stimuli. In this study, animals with maternal experience performed better than their virgin counterparts; in the most difficult phases of the experiment, the second-time mothers performed better than the first-time mothers—suggesting a parity effect (Higgins et al., 2007; Lambert & Kinsley, 2008). These results suggest that rats with maternal experience have the ability to alter foraging strategies in real time to respond to the changing demands of the environment. Moreover, their attention to detail in this past task appears to be better than nonmaternal animals.

In another attempt to understand the maternal animal's ability to alter foraging strategies in real time, food-restricted rats were exposed to a live cricket, a food source for feral rats. This task involves focused attention on the most salient features of the cricket stimulus and an ability to engage in coordinated movement to capture the moving prey. Maternal rats captured and killed the crickets in approximately 25% of the time required for the virgins to acquire the cricket. The sensory systems used in tracking and capturing a cricket are currently being explored to determine which sensory modalities, in addition to directed attention, facilitate cricket hunting in these laboratory maternal rats (Kinsley et al., 2006; Kinsley et al., submitted; Lambert & Kinsley, 2008).

In addition to enhanced foraging, altered responses in the face of environmental threats have been observed in maternal rodents. When placed in an elevated plus maze consisting of arms that are open and closed, more anxious animals prefer the closed arms (Pellow, Chopin, File, & Briley, 1985). In one study, pregnant rats spent more time in the open arms earlier in pregnancy (around Day 9) but not later in pregnancy (Day 18; Macbeth et al., 2008). Other studies, however, have reported mitigated anxious behavior later in the pregnancy (De Brito Faturi, Teixeira-Silva, & Leite, 2006). Focusing on the postpartum period accompanying lactation, anxiety has been observed to be consistently reduced (Byrnes & Bridges, 2006a, 2006b; Lonstein, 2007). Placed in an open field, first- and second-time maternal rats exhibited fewer behavioral signs of anxiety, accompanied by less brain activation in fear-related brain areas (Wartella et al, 2003). Long after weaning the pups, maternal animals were found to exhibit decreased anxiety in the elevated plus maze throughout their lives (Love et al., 2005).

Therefore, rodents experience changes in behaviors that appear to be ancillary to the more traditional parental responses, namely more efficient foraging and diminished anxiety. Do these observations extend to humans? As expected, the current literature suggests that the human female response is more complicated than observed in rodents. Focusing on the stress/anxiety response, as observed in the rats, decreased stress reactivity accompanies pregnancy in both physical and cognitive stress tests (De Weerth & Buitelaar, 2005). During lactation, dampened stress responses have been observed in response to exercise or a cold stressor; however, a mitigated stress response was found

in the social stress test only when the women breast fed minutes beforehand (Brunton & Russell, 2008; Brunton, Russell, & Douglas, 2008).

In addition to anecdotal evidence of incompetent mommy brains, research indicating that human brain volume shrinks during pregnancy suggests that the human literature may conflict with the rodent research portraying an enriched brain during pregnancy, lactation, and beyond (Oatridge et al., 2002), although this work also may mean that the brain is consolidating resources or contracting in preparation for expansion later on (as previously reported in the Kim et al. study). Postpartum human mothers and fathers, however, display higher levels of activity in limbic areas of the brain (known to be involved in emotional processing) when exposed to infant cries than nonparents, who respond more to laughter responses from infants (Seifritz et al., 2003). Although evidence of changes in brain activation in response to infant cues exists, cognitive enhancements are less apparent. There is disagreement, too, about the extent of the changes. One study, for example, reported negative cognitive effects such as forgetfulness, confusion, disorientation, and reading difficulties in pregnant professional women (Poser, Kassirer, & Peyser, 1986). During pregnancy, some studies show that various types of memory are compromised in women, including visual memory (Silber, Almkvist, Larsson, & Uvnas-Moberg, 1990), working memory (Janes, Casey, Huntsdale, & Angus, 1999), and attentional processes (Buckwalter, Buckwalter, Bluestein, & Stanczyk, 2011; Buckwalter et al., 1999). Glynn (2010) found pregnant women to exhibit diminished verbal recall memory, while recognition and working memory was not changed in comparison with healthy nonpregnant women. It is possible that the types of cognitive tasks being assessed in parous women fail to address the changes one expects to see in the maternal human. Additional studies, thus, are necessary to clarify this work.

Although scarce, some such research has been conducted. For example, human mothers find the body odors of infants more attractive than non-mothers (Corter & Fleming, 2002). In a direct comparison to the attention set-shifting paradigm described previously with maternal rats, human mothers have been exposed to a version of this test known as the Cambridge Neuropsychological Test Automated Battery. As observed in rats, human mothers demonstrating higher levels of infant sensitivity (e.g., adjusting interactions to maintain sustained communication with infant) made fewer errors than less sensitive mothers on the more difficult versions of the task requiring attentional shifts to new salient stimuli (Fleming, Gonzalez, Afonso, & Lovic, 2008). In addition to these neuropsychological studies in human mothers, qualitative research suggests that significant changes relevant for adaptive parental responses accompany the maternal experience. German policewomen, for example, have self-reported enhanced vigilance following the birth of their first child (Fullgrabe, 2002). Pearson, Lightman, and Evans (2009) reported that mothers apparently are more sensitive to emotional facial cues. Pearson's team examined facial expressions that depicted various emotional states by presenting pregnant women with images of other human faces. They asked them to rate the emotions expressed on those facial images and reported that, as pregnancy progresses, mothers become better at recognizing the emotions on the faces of others. The greatest recognition increase related to those faces exhibiting danger-anger (denoting a direct physical threat); disgust (connoting a possible contamination threat); and fear (perhaps of a visible threat). It would be interesting, therefore, to further investigate the effects of human motherhood on complex and adaptive functions in ethologically relevant settings.

CONCLUSION: LESSONS FROM THE PARENTAL BRAIN

As mammals arrived on the evolutionary scene, a host of complex social responses accompanied their entrance. These social responses, required for raising helpless mammalian offspring, coupled to less-than-reliable/available male partners, likely provided the fundamental basis of nurturing social responses such as empathy and caregiving in humans. These nurturing responses, best observed in maternal behaviors directed toward offspring, provide a unique opportunity to learn more about the brain's fascinating transition from a world consisting of "self" to one consisting of "self and other." As described in this tutorial, this transition requires substantial behind-the-scenes neurobiological efforts—including neurochemical, neuroanatomical, and neurophysiological modifications. Although the female brain appears to be more primed for nurturing parental responses, a select group of paternal species provides evidence that appropriate exposure to offspring also alters the male brain's response to young conspecifics. Consequently, our laboratories are currently exploring these effects in paternal models, a model characterized by less dramatic alterations in reproductive hormones. Learning more about how the mammalian brain initiates and maintains the plasticity required to meet the new demands of parenthood promises too to provide answers to neurobiological questions related to seemingly nonmaternal topics such as the emergence and regulation of neuroplasticity and adaptive social responses as well as a better understanding of the ramifications of a failure to adequately build the maternal brain.

AFFILIATIONS AND ADDRESSES

Kelly G. Lambert, Department of Psychology, Randolph-Macon College, Ashland, VA 23005, USA. E-mail: klambert@rmc.edu. Craig H. Kinsley is at the University of Richmond.

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