Hormones and Behavior 77 (2016) 86–97

Contents lists available at ScienceDirect

Hormones and Behavior

journal homepage: www.elsevier.com/locate/yhbeh

Neuroplasticity in the maternal hippocampus: Relation to cognition and effects of repeated stress

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ARTICLE INFO

Available online 27 June 2015

Keywords:
Hippocampus
Pregnancy
Lactation
Postpartum
Spatial memory
Depression
Steroid hormones
Parental brain

ABSTRACT

This article is part of a Special Issue "Parental Care".

It is becoming clear that the female brain has an inherent plasticity that is expressed during reproduction. The changes that occur benefit the offspring, which in turn secures the survival of the mother's genetic legacy. Thus, the onset of maternal motivation involves basic mechanisms from genetic expression profiles, to hormone release, to hormone–neuron interactions, all of which fundamentally change the neural architecture — and for a period of time that extends, interestingly, beyond the reproductive life of the female. Although multiple brain areas involved in maternal responses are discussed, this review focuses primarily on plasticity in the maternal hippocampus during pregnancy, the postpartum period and well into aging as it pertains to changes in cognition. In addition, the effects of prolonged and repeated stress on these dynamic responses are considered. The maternal brain is a marvel of directed change, extending into behaviors both obvious (infant-directed) and less obvious (predation, cognition). In sum, the far-reaching effects of reproduction on the female nervous system provide an opportunity to investigate neuroplasticity and behavioral flexibility in a natural mammalian model.

Introduction

Pregnancy and motherhood are accompanied by remarkable neurobiological changes. In a healthy mother, fluctuating changes in maternal steroid and peptide hormones during the peripartum period play a significant role in the onset of maternal behaviors, which are necessary for offspring survival (Bartels and Zeki, 2004; Bridges, 2014; Sheeman and Numan, 2002). Upon the arrival of the offspring, trial-and-error learning as a strategy to fine-tune maternal behavior is too-little, too-late. Although glimpses of maternal responsiveness such as tail carrying, nest building, and altered food preferences may be observed during pregnancy in the rat (Fleming, 2007; Lott and Rosenblatt, 1969; Rosenblatt, 1969, 1980), maternal behavior makes a rather abrupt appearance following parturition. In an almost seamless transition to the postpartum phase, maternal mammals engage in specific responses that are essential for offspring survival.

The transformation of an often offspring-aversive virgin animal to an offspring-seeking mother represents one of the most dramatic examples of behavioral flexibility in all of animal behavior. Rosenblatt and Mayer (1995) proposed an approach-avoidance model to explain this transition, suggesting that the motivation to avoid offspring, particularly in rats, is replaced by a competing motivation to approach offspring, post-parturition (Rosenblatt and Mayer, 1995). Interestingly, maternal responsiveness is not exclusive to postpartum rats considering that, even in virgin rats; a period of cohabitation with offspring will stimulate maternal responsiveness after about a week of exposure. Such pup-sensitized females engage in nest building, pup-grooming and crouching over the offspring, even in the absence of lactation (Rosenblatt, 1967). Pup exposure may reduce timidity in the virgins, enabling them to overcome social fears to interact with offspring (Fleming and Luebke, 1981). Maternal rats trained to bar-press to receive offspring, as well as a place preference for offspring-associated over cocaine-associated chambers, provide unequivocal evidence of the rewarding nature of offspring in postpartum females (Lee et al., 1999a; Mattson et al., 2003). An example of this extreme offspring-directed motivation is depicted in Fig. 1, in which a semi-free ranging adult female capuchin monkey was photographed carrying a young raccoon kit. With no males in the facility, the female capuchins were neither pregnant nor lactating, yet they still demonstrated motivation to gain access to offspring, even contra-specific offspring. This misdirected investment of energy in caring for offspring of another species (or conspecific competitors') serves as a vivid reminder of predisposed maternal neural circuitry underlying maternal motivation. This 'maternal circuit' involves such areas of the brain as the medial preoptic area,

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http://dx.doi.org/10.1016/j.yhbeh.2015.06.004
0018-506X/

Fig. 1. Contraspecific maternal motivation. Semi-free ranging capuchin female carrying a raccoon kit after abducting it from its natural mother.
Photo by Alex Huhman.

amygdala, prefrontal cortex, and nucleus accumbans (Lee et al., 1999b; Numan, 1988) (Fig. 2).

A tour of the maternal brain

In the case of the manifest changes that accompany the transition from nulliparity to pregnancy through maternity, a maternal brain is both the goal of the endocrine tsunami that accompanies pregnancy, and the culmination of millennia of natural selective processes. That the maternal brain is shaped by what may be termed enriching experiences, and that the responsivity to young remains with the parous female long after her actual production and care of young, suggests that an additional consequence of reproduction may be hitherto subtle cognitive improvements that accrue to the mother.

Previous work has described the maternal milieu as enriching (Kinsley et al., 2012a; Kinsley and Lambert, 2006; Kinsley et al., 1999; Kinsley et al., 2012b; Kinsley et al., 2006). For example, the factors that characterize the processes of pregnancy, production of young, and, critically, the flow of sensory information from the young back to the mother are rich, prolonged and significant (Fleming et al., 2002; Fleming et al., 1999). The cues from the offspring were believed to be more of a signaling device, a way to inform the mother that it was time to feed, or warm or retrieve the offspring. The cues certainly do this, but, as Kinsley et al. (2012a, 2012b) have argued, that is but the beginning. Rosenblatt pioneered the notion, with his classic 1967 paper, of pup stimuli alone – in the absence of pregnancy hormones – that cues from offspring could render a female rat maternally responsive merely with repeated exposure to the pup cues. Such sensitization or concaveation phenomena were sufficient to elicit maternal care from adult females (Cohen and Bridges, 1981). Such an effect likely involves mechanisms such as those reported by Engert and Bonhoeffer (1999), which involves the transduction of significant amounts of sensation into synaptic/neuronal remodeling via neuronal activation (Engert and Bonhoeffer, 1999). Therefore the amount of sensory information provided by the offspring – the sights, smells, sounds, tastes, somatosensory and suckling stimuli – must be significant and targeted. On the one hand, it helps to inform the mother as to the state of the offspring, requiring the proper response to the stimulus (a specific cry is met with a specific behavior; a particular odor with the proper amount of licking). On the other, the mother's brain is responding to these complex sensory stimuli by becoming structurally and functionally more complex.

The medial preoptic area (mPOA)regulates maternal motivation in a number of mammalian species (Levy, 2008; Numan et al., 2006; Perrin et al., 2007). For example, bar-pressing for offspring is diminished in rats with lesions in the mPOA, whereas stimulation here promotes pup-preferences in maternal females (Lee et al., 1999a; Morgan et al., 1999). Additionally, c-Fos immunoreactive cells are increased in both

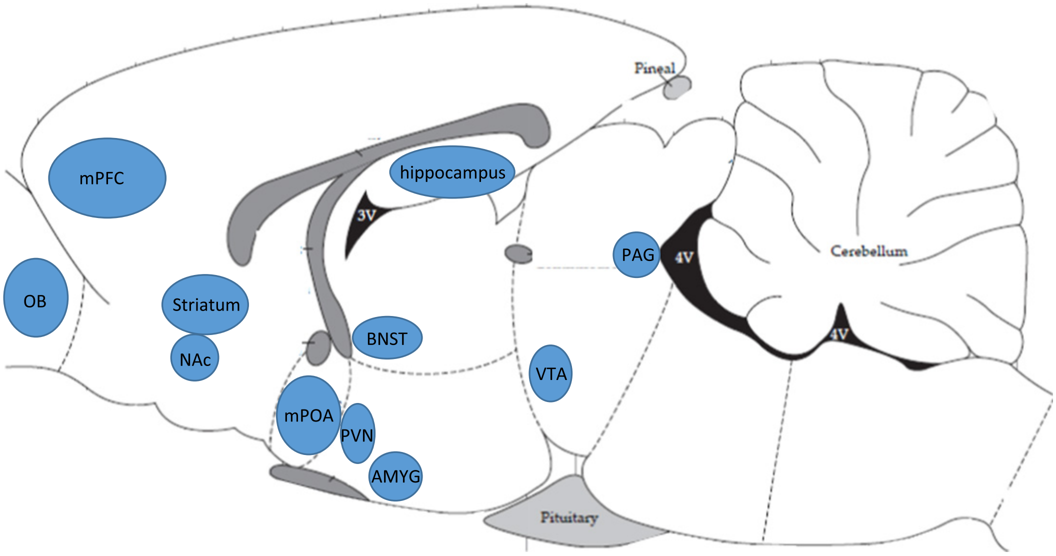

Fig. 2. Key brain areas important for maternal behaviors in the rat. AMYG, amygdala; BNST, bed nucleus of the stria terminalis; MPOA, medial preoptic area of the hypothalamus; NAc, nucleus accumbens; OB, olfactory bulb; PAG, periaqueductal gray; mPFC, medial prefrontal cortex; PVN, paraventricular nucleus of hypothalamus; VTA, ventral tegmental area. Brain schematic adapted from Paxinos and Watson (5th Edition).