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The birth of new neurons in the maternal brain: Hormonal regulation and functional implications

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ABSTRACT

The maternal brain is remarkably plastic and exhibits multifaceted neural modifications. Neurogenesis has emerged as one of the mechanisms by which the maternal brain exhibits plasticity. This review highlights what is currently known about peripartum-associated changes in adult neurogenesis and the underlying hormonal mechanisms. We also consider the functional consequences of neurogenesis in the peripartum brain and extent to which this process may play a role in maternal care, cognitive function and postpartum mood. Finally, while most work investigating the effects of parenting on adult neurogenesis has focused on mothers, a few studies have examined fathers and these results are also discussed.

1. Introduction

Becoming a mother is one of the most monumental events in a female's life. Across mammalian species, major hormonal shifts during pregnancy, parturition and the postpartum period coupled with experiential factors modify the brain and, as a result, the behavior of the female producing a high level of maternal responsiveness along with changes in maternal mood, cognition and stress regulation (Fleming et al., 1999; Numan and Insel, 2003; Lonstein, 2007; Slattery and Neumann, 2008; Macbeth and Luine, 2010; Numan and Woodside, 2010; Workman et al., 2012; Dulac et al., 2014; Galea et al., 2014; Hillerer et al., 2014; Perani and Slattery, 2014; Rilling and Young, 2014; Pereira and Ferreira, 2015). Together, these changes represent adaptive responses that are necessary to ensure the survival and well-being of the offspring.

The neural modifications found in the maternal brain are numerous and widespread (Fig. 1) consisting of neurochemical, neuroendocrine, activational, morphological, gene expression and functional changes within a distributed but interconnected circuitry (Theodosis et al., 1986; Xerri et al., 1994; Featherstone et al., 2000; Keyser-Marcus et al., 2001; Tomizawa et al., 2003; Rasia-Filho et al., 2004; Febo et al., 2005; Miranda and Liu, 2009; Sanna et al., 2009; Leuner et al., 2010; Canavan et al., 2011; Salmaso et al., 2011a, 2011b; Lonstein et al., 2014; Bridges, 2015; Cohen and Mizrahi, 2015; Corona and Levy, 2015; Elyada and Mizrahi, 2015) that includes the hypothalamus, amygdala, nucleus accumbens, olfactory bulb, hippocampus and various cortical areas (i.e. parietal, auditory, somatosensory, prefrontal). Within distinct areas of this circuitry, adult neurogenesis has emerged as another important mechanism that contributes to maternal neuroplasticity (Leuner et al., 2010; Levy et al., 2011; Galea et al., 2014; Pawluski et al., 2015b; Slattery and Hillerer, 2016) and will be the focus of this review.

2. Neurogenesis in the adult brain

Neurogenesis is the process by which new neurons are generated from neural stem cells or progenitor cells. In most adult mammals, neurogenesis primarily occurs in two main regions, the dentate gyrus (DG) of the hippocampus and the olfactory bulb (OB) (Ming and Song, 2011; Aimone et al., 2014; Lepousez et al.,

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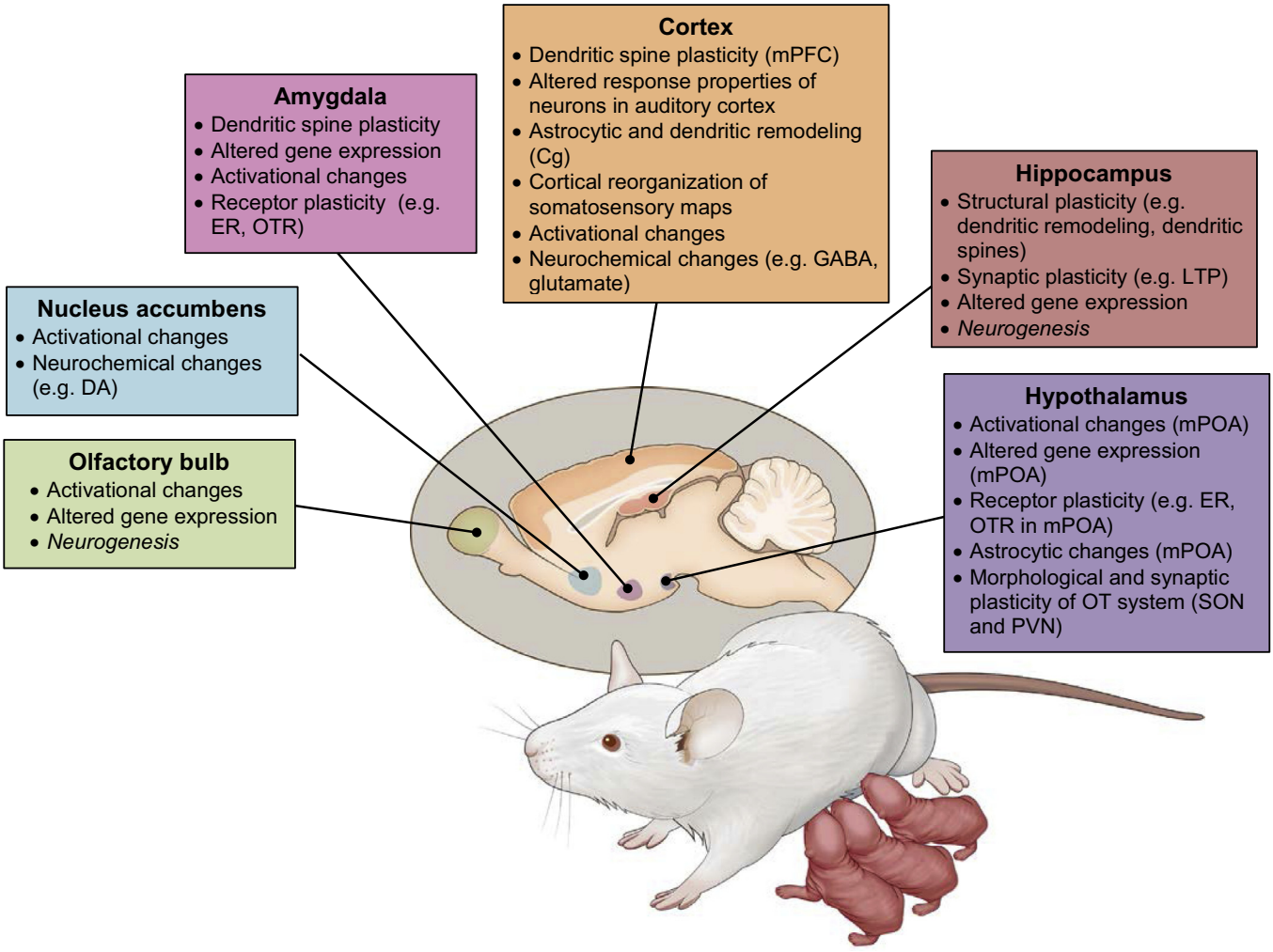

Fig. 1. Schematic diagram highlighting various modifications in the maternal brain. DA = dopamine, ER = estrogen receptor, OTR = oxytocin receptor, mPFC = medial prefrontal cortex, Cg = cingulate cortex, LTP = long term potentiation, mPOA = medial preoptic area, PVN = paraventricular nucleus, SON = supraoptic nucleus.

2015). Within the DG and OB, neurogenesis is a multi-step process that includes proliferation, migration, survival, differentiation and integration of newborn neurons into the existing circuitry (Leuner and Gould, 2010; Ming and Song, 2011). In the OB (Fig. 2a), newly-born cells originate from the sub-ventricular zone (SVZ) which lies adjacent to the wall of the lateral ventricle. Neural progenitor cells residing in the SVZ give rise to transient amplifying cells which differentiate into neuroblasts. These neuroblasts then migrate a great distance along the rostral migratory stream (RMS) to reach the OB where they become mostly local inhibitory interneurons which join the neural networks of the olfactory system to participate in a range of odor-guided behaviors (Gheusi et al., 2013; Lepousez et al., 2015). In the DG (Fig. 2b), neural progenitor cells proliferate in the sub-granular zone (SGZ) and give rise to neuroblasts that migrate a short distance into the granule cell layer (GCL) where a percentage will survive and mature, becoming glutamatergic granule neurons that synaptically and functionally integrate into the neuronal network of the hippocampus to play a role in cognition, mood and stress regulation (Leuner and Gould, 2010; Snyder et al., 2011; Aimone et al., 2014; Cameron and Glover, 2015).

In both neurogenic brain regions, adult born neurons serve as excellent candidates for plasticity during pregnancy, parturition and the postpartum period because they are not only sensitive to many hormonal and experiential changes that occur during these times but also because the functions which they have been suggested to contribute to are affected by motherhood. Here we highlight similarities and differences in the effects of motherhood on adult neurogenesis in the DG and SVZ across various species as well as the putative underlying mechanisms. We also consider the extent to which neurogenesis in the peripartum SVZ and/or DG may play a role in maternal care, cognitive function and postpartum mood. Finally, while most work investigating the effects of parenting on adult neurogenesis has focused on mothers, a few studies have examined fathers and these results are also discussed (Leuner et al., 2010; Levy et al., 2011; Lieberwirth and Wang, 2012).

3. Important considerations

Studying a dynamic process like adult neurogenesis during dynamic periods such as pregnancy and the postpartum period is inherently complex. New neurons are born, develop and mature while mothers are carrying or caring for offspring who are doing the same all the while undergoing numerous physiological changes. An additional level of complexity arises when attempting to compare species which can differ with respect to variables such as reproductive strategy, degree of parental investment, developmental maturity of offspring at birth as well as certain temporal features of adult neurogenesis (Snyder et al., 2009; Bonfanti and Peretto, 2011; Lieberwirth and Wang, 2012; Brus et al., 2013). Even