·Research Highlight·

The medial preoptic area and the regulation of parental behavior

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The preoptic area (POA) is located in the most anterior part of the hypothalamus and is bordered dorsally by the anterior commissure and anteroventrally by the nucleus of the diagonal band of Broca[1]. Accumulating evidence from developmental neurobiology suggests, however, that the POA may be a separate entity from hypothalamus, and may actually be part of the basal telencephalon[2, 3]. Both the hypothalamus and POA are highly complex and heterogeneous areas, containing multiple nuclei, each of which has specific fundamental functions for survival. Among these, the POA contains nuclei involved in the regulation of blood osmolality and temperature (the median preoptic nucleus), sleep (the ventrolateral preoptic and suprachiasmatic nuclei), ovulation (gonadotropin-releasing hormone neurons scattered mainly in the ventral part of the POA), male sexual behavior (the medial preoptic nucleus), and parental behavior (the central part of the medial POA, cMPOA).

Parental behavior in mammals is typically a uniparental maternal care system, while paternal and alloparental behaviors (parental responses toward infants that are not one's biological offspring) are not common. However, paternal and alloparental behaviors do occur in those species where such behaviors have adaptive significance[4, 5].

A critical role of the medial POA (MPOA) in maternal behavior was initially suggested by Fisher[6], and has been established in a series of studies by Numan[7, 8] in laboratory rats. Then it was confirmed in other rodents, such as hamsters[9], California mice[10], and laboratory mice[11], as well as for paternal and alloparental behaviors[10–13]. The MPOA is also involved in the parental behavior of sheep[14] and presumably most other mammals. Severing the lateral, in particular the dorsolateral, connections of the MPOA disrupts maternal behavior most strongly and specifically, compared to cutting the anterior, posterior, or dorsal connections[15, 16]. These findings are consistent with the fact that the major afferent and efferent connections of the rat medial preoptic nucleus, the largest and central nucleus of the MPOA, enter and leave laterally[17].

While postpartum maternal behavior is similar in laboratory rats and mice, alloparental behavior in virgin animals differs quite impressively. Virgin female rats initially avoid, and may even attack, young pups, and they require several days of continuous pup exposure (sensitization) before their behavior switches toward displaying parental responses[18]. Virgin male rats behave similarly[18]. In contrast, the majority of virgin female mice start retrieving pups and showing other parental responses within 30 to 60 min after their first exposure to pups[19]. In other words, nulliparous female laboratory mice, unlike most female mammals, do not require pregnancy hormones or extensive pup sensitization to induce immediate maternal care. In contrast to their female counterparts, virgin male laboratory mice behave more like virgin female and male rats, and are more avoidant or even infanticidal on their first exposure to pups[20]. Significantly, once these male mice become fathers by mating and cohabitation with their pregnant mates, they show extensive paternal care toward their offspring as well as non-offspring pups[21]. The underlying mechanism for this behavioral switch induced by social experience with the female mate is unknown, although it has been shown that surgical removal of the vomeronasal organ abolishes the infanticidal response and turns virgin male mice toward parental responsiveness[22]. Interestingly, vomeronasal organ removal also facilitates maternal behavior in virgin female rats[23], and decreases infanticide in male rats[24].

It appears that dual neural mechanisms regulating behavioral responses toward infants exist in the brains of most male and female rodents: typical virgin females and males initially avoid pups, while postpartum females, and males of certain species that have mated and cohabitated with females, care for the young. In comparison to most mammals, the spontaneous maternal behavior of virgin female laboratory mice is atypical; indeed, feral female virgin mice are infanticidal[8] (see [4, 5] for a broader analysis of these issues).

Recently, Wu and colleagues reported on the role of galanin neurons in the MPOA for parental behavior in both male and female mice[25]. They showed that (1) virgin male mice lacking the *Trpc2* gene, which encodes a vomeronasal-organ-specific ion channel, show paternal behavior rather than infanticide; (2) Galanin, a neuropeptide widely expressed in the brain, spinal cord, and gut, is co-expressed with c-Fos induced in MPOA neurons by parental behavior (38.3% of MPOA c-Fos-positive neurons co-express galanin, and 24.8% of MPOA galanin-positive neurons co-express c-Fos in virgin females displaying parental behavior), consistent with a previous publication (47.7% and 29.6%, respectively, in the cMPOA)[11]; (3) ablation of the galanin neurons within the MPOA causes impairments in parental behavior and male mating behavior; and (4) optogenetic stimulation of MPOA galanin neurons attenuates infanticide and inter-male aggression in virgin males, and facilitates pup grooming (sniffing and licking) as well as general locomotion at the expense of crouching behavior. The strength of this study is the specific manipulation of galanin neurons using a galanin-cre mouse line in combination with sophisticated virus-vector-mediated gene-transfer techniques. Such approaches will become indispensable tools for elucidation of the neuronal circuits of the mammalian parent-infant relationship.

The functional role of galanin is largely unknown, however; it has been implicated in diverse biological processes including lactation *via* prolactin secretion, neural development, feeding, mood regulation, and osmoregulation (see [26] for review). Moreover, galanin expression is widely distributed in the MPOA. As such, it is reasonable to assume that the manipulation of MPOA galanin neurons affects not only pup-directed behaviors but also other behaviors and physiological functions. More anatomically-specific targeting of experimental manipulations within subregions of the MPOA in future studies should provide more information on the neuronal basis of pup-directed behaviors in relation to other social behaviors, in particular the behavioral switch from infanticide to paternal care in male mice that is induced by social interactions with females. Perhaps one population of MPOA neurons is involved in suppressing an avoidance/infanticide circuit, while another population is involved in stimulating a parental circuit[4, 27]. Significantly, the facts that Wu *et al.*[25] found that stimulation of MPOA galanin neurons in virgin males reduces infanticide without stimulating parental behaviors, while ablation of these neurons in fathers and postpartum females suppresses parental behavior without inducing infanticide, support the view that there are two functionally distinct MPOA ~~galanin~~ populations. Obviously, much more research needs to be done to determine, for example, which functional aspects of parental behavior are regulated by MPOA galanin neurons, and whether the critical MPOA-galanin neurons are local-circuit neurons, output projection neurons, or both.

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