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Review

Neuroendocrine regulation of maternal behavior

Robert S. Bridges *

Department of Biomedical Sciences, Neuroscience and Reproductive Biology Section, Tufts University – Cummings School of Veterinary Medicine, North Grafton, MA 01536, USA

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ABSTRACT

The expression of maternal behavior in mammals is regulated by the developmental and experiential events over a female's lifetime. In this review the relationships between the endocrine and neural systems that play key roles in these developmental and experiential processes that affect both the establishment and maintenance of maternal care are presented. The involvement of the hormones estrogen, progesterone, and lactogens are discussed in the context of ligand, receptor, and gene activity in rodents and to a lesser extent in higher mammals. The roles of neuroendocrine factors, including oxytocin, vasopressin, classical neurotransmitters, and other neural gene products that regulate aspects of maternal care are set forth, and the interactions of hormones with central nervous system mediators of maternal behavior are discussed. The impact of prior developmental factors, including epigenetic events, and maternal experience on subsequent maternal care are assessed over the course of the female's lifespan. It is proposed that common neuroendocrine mechanisms underlie the regulation of maternal care in mammals.

1. Introduction

In recent years our understanding of the relationships between neural and endocrine systems in the regulation of maternal behavior has received considerable research attention. Roles for specific hormones, neurochemicals, and brain regions involved in the induction, maintenance, and retention of maternal care in mammals have been identified. These chemical systems and anatomical substrates are discussed here within the context of development and the female mammal's reproductive life history.

In order to provide an understanding of the relationships between maternal behavior and its biological control, it is important to place the broader players within a conceptual context. Whereas it is commonly considered that the control of maternal behavior has a neuroendocrine basis (Bridges and Byrnes, 1999), it is equally accurate to conceptualize the relationship between the brain and the endocrine system as an endocrine-neurological link. This construct was first brought to my attention by the neuroendocrinologist Dr. Joseph Martin, past Dean of Harvard Medical School, in a seminar he presented in the late 1980s on growth hormone regulation and action. As depicted in the schematic in Fig. 1 and elucidated within this review, the actions of hormones from both the pituitary and other peripheral endocrine tissues play a crucial role in feeding back upon sites within the central nervous system, many within the hypothalamus, to regulate the female's responses to young and related stimuli. Hence, the regulation of maternal behavior is as much of an endocrine-neurological process as it is a strictly neuroendocrine mediated event.

The aim of this review is to present the existing framework of the underlying neuroendocrine foundation in the regulation of maternal behavior. Whereas most of the research findings focus on studies in rats and mice, attention to other species, including humans, complements the more expansive data set in rodents. Possible common regulatory mechanisms are considered in light of the normative behavioral responses of the given species.

2. Maternal behavior

2.1. Maternal responses

Responses or behaviors displayed by the female that specifically support the development and growth of her offspring constitute a set of responses termed maternal behaviors. The capacity to respond maternally appears to be present throughout development from the pubertal period into adulthood. However, the intensity and incidences of maternal responses are most pronounced beginning at the time of birth. At parturition the new mother displays both an intense interest in the amniotic fluids and the young together with an enhanced motivation to respond positively to her newborn.

* Address: Department of Biomedical Sciences, Tufts Cummings School of Veterinary Medicine, 200 Westboro Road, North Grafton, MA 01536, USA. Fax: +1 508 839 8740.
E-mail address: robert.bridges@tufts.edu

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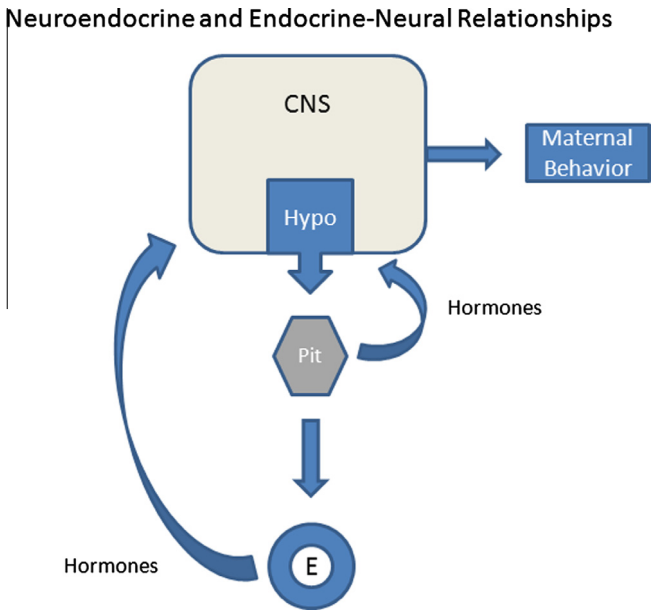

Fig. 1. Schematic of the overall relationships between the brain and components of the endocrine system in the regulation of maternal behavior. The actions of hormones secreted by the pituitary (Pit) gland or peripheral endocrine (E) tissues, such as the ovaries, adrenal glands, and placenta, act upon key neural sites within the hypothalamus (Hypo) and other brain regions in the central nervous system (CNS) to stimulate and modulate the expression of maternal behavior. Moreover, intrinsic neurochemical systems within the hypothalamus that are regulated by hormones as well as sensory inputs act centrally to affect maternal care. The actual "neuroendocrine" link between the Hypo and the Pit mediates the release and subsequent actions of neuroactive hormones as part of a feedback system or loop.

What are the maternal responses that emerge at birth and are expressed during the development of her offspring throughout lactation and beyond? In preparation for birth, expectant mothers display increased levels of aggression towards intruders as well as increased nest building (Mayer and Rosenblatt, 1984). At birth most newly parturient mothers ingest amniotic fluid and consume the placenta. These behaviors are thought to provide a source of nutrition for the mother as well as remove a potential olfactory attractant of the afterbirth to predators. The placenta is a rich source of hormones that appear to facilitate lactogenesis and decrease the energetic load on the mother. Maternal responses following birth, in general, can be grouped into two categories, those directed at the young and those indirectly related to the young. These behaviors are listed in Table 1. In rodents, young-directed responses include behaviors such as retrieval, pup-licking and grooming, crouching, and active nursing. Non-directed maternal behaviors include protection of the young or maternal defense, nest building, increased food consumption, i.e. lactational hyperphagia, and diminished anxiety with associated increases in exploratory activity.

Maternal responses are set within the behavioral framework of the female. For example, while retrieval is a common behavior displayed by rodents, cats and dogs, in sheep maternal bleats and proximity to young availing access to the utter are characteristic maternal responses. In non-human primates, carrying young and physical closeness are considered important components of maternal care. In humans, visual "en face" contact with babies as well as assessments of attachment, mood state, and olfactory recognition are used as endpoints to measure maternal state. Given the context of behavioral responses across a range of mammals, it makes comparisons of underlying neuroendocrine mechanisms with biological regulators across species challenging. One assumption made in evaluating the neurobiological bases of maternal behavior is that similar, albeit not identical, mechanisms regulate functionally common behavioral responses.

In general, assessment of maternal capacity has typically used measurements of young-directed responses. In rats and mice, for example, latencies and incidences to retrieve and group young in the nest have been utilized to assess the neurobiological capacity of females to display maternal behavior. The basic neurobiological capacity in females to respond in a maternal fashion towards young is present throughout development from the prepubertal period into older age. In prepubertal juvenile female rats maternal-like responses are displayed after exposure to foster young for a day or two (Bridges et al., 1974). Response latencies toward foster young subsequently increase to 5–6 days in adulthood (Rosenblatt, 1967), latencies that appear to be maintained throughout adult life in female rats that do not give birth. These response latencies decline during late pregnancy with shortened latencies present prepartum (Slotnick et al., 1973). At birth, the new mother displays a spontaneous set of pup-directed behaviors. Once these behaviors are established, they persist at an enhanced level throughout the remainder of adult life (Bridges, 1975; Bridges and Scanlan, 2005; Scanlan et al., 2006).

The majority of studies that have examined the indirect-young associated maternal response of maternal defense or maternal aggression have conducted research using rodent models. Maternal aggression in lactating rats is most pronounced during the first week postpartum (Erskine et al., 1978). When an intruder is introduced into the home cage of the lactating rat, the female displays an increased incidence of a set of responses. This behavior consists of frontal and lateral attacks, rearing, biting, kicking, and upright boxing (Lonstein and Gammie, 2002). Recent studies have further demonstrated that during a second lactation, the intensity of maternal defense in response to a male intruder is greater than that found in age-matched, lactating primiparous dams (Nephew et al., 2010). Although the specific components and incidences of maternal defense may vary, the overall behavioral ethograms are similar across mammals. A second significant shift in non-pup directed behavior associated with pregnancy and lactation involves increases in food consumption together with a temporally related state of leptin resistance (Ladyman and Grattan, 2005). The neurobiological underpinnings of maternal defense and the regulation of energy balance are discussed later in this article.

One perspective that is important to maintain is that the mother's response to young is contextually driven. That is, her behaviors towards young are dependent upon the stimuli in her immediate environment and involves motor responses that are regulated by alterations in her motivational and reward states that are formed over her lifetime of and a product of the interactions between underlying biological determinants and experiential events. Simplistically stated, at parturition the new mother attends to the immediate set of new stimuli such as amniotic fluid, the

Table 1
Maternal related-behaviors.

Parturitional responses
Stimulation of newborn
Consumption of amniotic fluid
Placentophagia
Young directed responses
Retrieval – maximizing contact with young
Licking and grooming
Nursing/crouching
Providing warmth and safety/nest building
Young related responses
Protection of the young – maternal aggression
Increased food consumption
Reduced anxiety to enhance exploratory activities