Neuroscience and Biobehavioral Reviews xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Neuroscience and Biobehavioral Reviews

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

Review

New theoretical and experimental approaches on maternal motivation in mammals

Daniel E. Olazábal[a,*], Mariana Pereira[b], Daniella Agrati[c], Annabel Ferreira[c], Alison S. Fleming[d], Gabriela González-Mariscal[e], Frederic Lévy[f], Aldo B. Lucion[g], Joan I. Morrell[b], Michael Numan[h], Natalia Uriarte[i]

[a] *Departamento de Fisiología, Facultad de Medicina, Universidad de la República, Avda. Gral. Flores 2125, CP 11800, Montevideo, Uruguay*
[b] *Center for Molecular and Behavioral Neuroscience, Rutgers, The State University of New Jersey, NJ, United States*
[c] *Sección Fisiología y Nutrición, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay*
[d] *Department of Psychology, University of Toronto at Mississauga, Mississauga, ON, Canada*
[e] *Centro de Investigación en Reproducción Animal, CINVESTAV-Universidad Autónoma de Tlaxcala, Tlaxcala, Mexico*
[f] *INRA, UMR 7247, CNRS/Université F. Rabelais/IFCE, Nouzilly, France*
[g] *Departamento de Fisiologia, Instituto de Ciências Básicas da Saúde, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*
[h] *Department of Psychology, Boston College, Boston, MA, United States*
[i] *Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay*

ARTICLE INFO

Article history:
Received 8 November 2012
Received in revised form 17 March 2013
Accepted 8 April 2013

Keywords:
Appetitive/consummatory behaviors
Behavioral switching
Dopamine
Maternal behavior
Motivation
Mouse
Proactive/passive behaviors
Rabbit
Rat
Sheep
Voles

ABSTRACT

Maternal behavior is expressed in different modalities, physiological conditions, and contexts. It is the result of a highly motivated brain, that allows the female to flexibly adapt her caring activities to different situations and social demands. To understand how mothers coordinate maternal and other motivated behaviors we discuss the limitations of current theoretical approaches to study maternal motivation (e.g. distinction between appetitive and consummatory behaviors), and propose a different approach (i.e. motorically active vs. passive motivations) and a distinction between maternal motivated *state* and maternal motivated behaviors. We review the evidence supporting dopamine mediation of maternal motivation and describe how different phases of the dopaminergic response – basal, tonic, and phasic release in the nucleus accumbens – relate to increased salience, invigorating behavior, and behavioral switching. The existing and new experimental paradigms to investigate maternal motivation, and its coexpression and coordination with other social or non-social motivations are also analyzed. An example of how specificity of motivational systems (e.g. maternal and sexual behavior at postpartum estrus) could be processed at the neural level is also provided. This revision offers new theoretical and experimental approaches to address the fundamental question of how mothers flexibly adapt and coordinate the different components of maternal behavior with other motivated behaviors, also critical for the survival of the species.

Contents

---

* Corresponding author. Tel.: +598 2924 3414x3531; fax: +598 2601 1211.
E-mail addresses: neurolazabal@hotmail.com (D.E. Olazábal), pereiram@andromeda.rutgers.edu (M. Pereira), dagrati@fcien.edu.uy (D. Agrati), anna@fcien.edu.uy (A. Ferreira), alison.fleming@utoronto.ca (A.S. Fleming), gglezm@prodigy.net.mx (G. González-Mariscal), levy@tours.inra.fr (F. Lévy), alucion@ufrgs.br (A.B. Lucion), jmorrell@andromeda.rutgers.edu (J.I. Morrell), michael.numan@bc.edu (M. Numan), natiuria@fcien.edu.uy (N. Uriarte).

0149-7634/$ – see front matter
http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

1. Introduction

Parental behavior is the result of complex internal processes and external factors that ensure that an individual takes care of the young, contributing to their survival by providing food, warmth, shelter, protection from predators and conspecifics, and appropriate stimulation. In mammals, lactating females are commonly responsible for providing all these benefits but, depending on the reproductive strategy of each species, males and other family members can also contribute to the care. In this context, mothers also interact socially with other members of their family or social group, besides their offspring. A flexible caregiving strategy by the mother requires a highly motivated and flexible brain to adapt to the different social contexts. These are the topics that brought the authors of this review together to participate in a Workshop that took place in Montevideo, Uruguay on September 3–5 of 2011. The workshop entitled *Neural basis of maternal motivation: relationship and coordination with other social motivational systems* was co-organized by Daniel Olazábal and Mariana Pereira. The aim of this workshop was to discuss how the brain adapts to and regulates maternal behavior in different species, and physiological and social conditions. The results of those discussions and of the academic exchanges that continued since then are presented in two separate reviews. The first review focuses on theoretical and experimental aspects of maternal motivation and the second review on the neural basis that supports the different forms and modalities of maternal behavior across mammals. Both of these reviews emphasize the mechanisms that provide flexibility and adaptation to the system. In the first two sections of the present review, we introduce the topics discussed at the Workshop and summarize the mechanisms of onset, maintenance and decline of maternal responsiveness in parturient and naive cycling animals and briefly describe the complex challenges of motherhood. In the third section we discuss the advantages and limitations of applying a number of concepts that are extensively used in the literature on behavioral motivation, to our studies on maternal motivation. In particular, we critique the distinction between appetitive and consummatory behaviors in the maternal behavior system, and propose new approaches and experimental models to study maternal motivation. We also put the existing evidence related to maternal motivation in the context of current theoretical interpretations of motivational processes (i.e. incentive salience, wanting vs. liking, etc.). In Section 4, we present a series of studies that investigates maternal motivation, either by manipulating or measuring the hormonal milieu or the dopaminergic system, and integrate and discuss these findings with the new theoretical approaches proposed in Section 3. Section 5 describes some examples of the coexpression, coordination and switching between maternal and other motivations, and propose experimental approaches to understand its neural basis. Section 6 discusses the specificity of motivational neural systems underlying sexual and maternal motivation, in particular at the postpartum estrus. Finally, the last section brings the discussion full circle, where we summarize the main points that have come out of these discussions and raise some of the future challenges in the maternal behavior field.

2. Maternal behavior in parturient and naïve cycling animals

Parental behavior is essential for the survival of mammalian species, in which females are most commonly responsible for taking care of the offspring. The majority of lactating mammals share many behavioral features; they consume placenta, fetal membranes and amniotic fluids, clean off the neonates, exhibit a selective interest in the young and respond maternally to them, while at the same time defending the offspring from intruders or predators, for example when showing aggressive behavior (Numan et al., 2006).

The motivation to display parental behavior is very high at the time of parturition, when females (and in some cases males) show a very rapid interest in the newborn. In most rodents (e.g. rats, mice, hamsters) and primates, the mother builds a nest, transports or retrieves the newborn to the nest, cleans and licks them and adopts nursing postures (Numan and Insel, 2003).

However, in some species like the prairie voles, california mice, or marmosets, the father or other members of the family group assist the lactating female in the care of the young (Numan and Insel, 2003), indicating that maternal behavior can also emerge under different physiological and social contexts. For instance, virgin female rats eventually become maternal after several days of continuous exposure to foster newborn (Cosnier, 1963; Rosenblatt, 1967). This process (called pup-induction or sensitization of maternal behavior) leads to a pattern of behavior very similar to that of the lactating mother (Numan et al., 2006). During that continuous exposure to foster newborn, the animal often must overcome an initial aversion to pups before they approach, contact and start displaying all components of maternal behavior (Fleming et al., 1989). On the other hand, some non-lactating rodents (e.g. prairie voles) and primates (e.g. marmosets, humans) readily interact with newborns, displaying immediate maternal or paternal behavior without needing a prior period of sensitization (Kuroda et al., 2011; Lucas et al., 1998; Olazábal and Young, 2005).

2.1. Onset, maintenance, and offset of maternal behavior

Some of the behaviors typically displayed by mothers begin during pregnancy, like the construction of a maternal nest (González-Mariscal et al., 1994), and the preference for pup odors

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

(Bauer, 1983; Fleming et al., 1989; González-Mariscal and Chirino, 2011; Kinsley and Bridges, 1990; Lévy et al., 1983). Therefore, there are intrinsic factors that make newborns attractive for the mother, so the parturient animal does not need to learn or interact with the newborns to find them attractive. This attraction develops at the end of pregnancy or around parturition, when a significant change occurs in the motivational value of sensory cues associated with the pups. This increase in the sensitivity and attraction for pup-related stimuli promotes mother–offspring interaction, which in turn allows other stimuli (e.g. tactile) to strengthen maternal behavior, maintaining it throughout lactation in the absence of the hormonal profile typical of the end of pregnancy.

Estradiol (E2) and progesterone (P4) are essential for stimulating maternal behavior at the end of pregnancy in many species (González-Mariscal et al., 1996; Numan et al., 2006). Increased ratio of E2/P4, and prolactin and oxytocin release into the brain around parturition are associated with the onset of maternal behavior in rats, sheep, and some primates, among other species (Bridges, 1996; Da Costa et al., 1996; González-Mariscal and Poindron, 2002; Kendrick et al., 1987; Lévy et al., 1992; Numan et al., 2006; Pedersen and Prange, 1979; see also Olazábal et al., 2013).

Hormonal profiles typical of the end of pregnancy change drastically around delivery and throughout lactation (for reviews see: González-Mariscal and Poindron, 2002; Numan et al., 2006). There is extensive evidence (Rosenblatt and Siegel, 1981) supporting the existence of a transition period from a hormonal control to a somatosensory regulation of maternal behavior after parturition. The separation of the mother and the young at parturition (or the immediate postpartum period) provokes long-lasting alterations in maternal behavior, especially in primiparous females (González-Mariscal and Poindron, 2002; Numan et al., 2006). Thus, across lactation, and after the hormonal events that stimulated maternal behavior at parturition have waned, the unfailing species-specific expression of maternal behavior is mostly maintained by particular forms of stimulation coming from the young. Some positive incentive stimuli (stimuli that can trigger motivated responses) from the young are unconditioned and elicit attractive responses by themselves (Kinsley and Bridges, 1990), while others require motor and sensory interaction to allow for the enhancement of the positive incentive values of young for the mothers. In both cases, the interaction with the pups maintains and enhances their attractive value. As the newborn get older, maternal behavior declines, the young spend more time exploring out of the nest, or eating solid food (Cramer et al., 1990), and mothers eventually avoid the suckling attempts of the pups. These behavioral changes lead to the cessation of nursing and subsequent weaning (Cramer et al., 1990; Reisbick et al., 1975). However, the incentive value of stimuli from younger pups is not lost at weaning, as newborns can stimulate appropriate maternal responses in late postpartum females (Reisbick et al., 1975).

3. Theoretical and experimental paradigms for studying maternal motivation

Mothers not only take care of the offspring but also perform other social and non-social activities. In many species for example, maternal females display sexual behavior at the postpartum estrus, and spend significant amount of time foraging. Maternal females can also share the caring of the young with other females, and maintain non-aggresive or aggresive interactions with other members of their family group adapting her caring activities to the context. This requires a flexible caregiving strategy by the mother and a highly motivated and flexible brain to adapt to those different social and environmental contexts. Current concepts in the motivational field do not consider this complexity. Therefore, in this section we discuss some advantages and limitations of common definitions of motivation, theoretical concepts, and experimental paradigms to understand maternal motivation.

3.1. *What is maternal motivation?*

Care-taking activities result from neural processes that mediate the attraction to newborns and regulate the proximity and interaction with them. These processes are known as maternal *motivation* (Latin: to move, or reason to move), and are reflected in the investment of time and resources to seek and maintain contact with the young (Numan and Woodside, 2010; Pereira and Morrell, 2011). Different definitions of motivation have emphasized different aspects of these behavioral processes, and therefore, have differently contributed to, or influenced, the research carried out by the scientific community in the behavioral motivation area. For example, motivation is commonly defined as an internal process that modifies the way an organism responds to a certain class of external stimuli (Pfaff, 1982). This internal process would make animals become aroused and direct their attention and behavior toward particular stimuli, for example, by changing the incentive value that a newborn has for a pregnant female even before delivery. This definition has been particularly useful to investigate the onset of maternal behavior at the end of pregnancy and the proactive components of maternal behavior (Lee et al., 1999; Numan and Woodside, 2010; Pereira and Morrell, 2011). This type of definition of motivation, however, emphasizes a *change or modification* in the perception of certain stimuli.

Other authors have postulated motivation as the potential for behavior that is built into a system of behavioral control (Buck, 1999). Buck (1999) proposes that neural and chemical systems exist for different motivations, but those are only manifested under appropriate conditions. For example, organisms would have intrinsic, hard wired or built-in mechanisms to respond maternally when exposed to newborns to ensure the survival of the species. When the appropriate conditions are present, these *purpose* systems are activated and species-specific maternal behavior ensues. In contrast to Pfaff's (1982) definition, Buck and others (see Kelly, 2004) emphasizes the control and expression (or *read out*) of behavior and emotional/affective experiences rather than the modification of the perception of a certain stimulus. Thus, Buck's definition also includes the rapid triggering of intrinsic behavioral responses that are built into the brain to be expressed when the appropriate context or stimuli are present and/or when rapid changes in the internal state unblock their expression. In summary, the latter definition assumes that certain intrinsic behavioral responses can be expressed when the animal encounters an appropriate context and therefore, there need not occur the modifying of an existing (for example inhibitory) behavioral response to that stimulus. We think these two definitions are complementary and one way to harmonize them is to consider that these internal processes (that filter the expression of behavioral responses) can be activated either slowly (e.g. hormonal priming or habituation to pup' odors) or immediately (in seconds or minutes) when the appropriate stimulus/contextual condition (e.g. sudden changes in internal drives, presence of newborn) is present. The use of this harmonized definition will allow us to include in our analysis two main neural processes that mediate maternal behavior and motivation; (1) the maternal motivated 'state' that selectively increases the probability that the animal will perform maternal behavioral components, and (2) the maternal motivated choice and execution of the appropriate behavioral components (retrieval, nursing, licking, nest building, etc.) that ensures that the animal adapts its behavior to the context and the specific environment encountered (Fig. 1). That is, once the animal is 'maternally motivated' (motivational *state*), as occurs at the end of pregnancy in rats and other species,

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

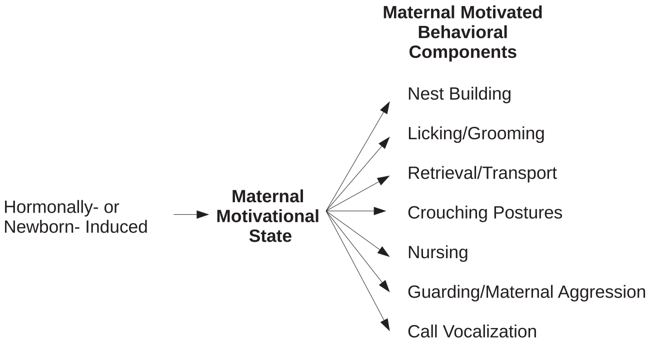

Fig. 1. Main distinction between a maternal motivational *state* (induced by hormones or cohabitation with newborns) and the different maternal motivated behavioral components that are selected (among other behaviors) under that condition.

it must quickly (in seconds or minutes) select and express specific motivated behavioral choices once the newborn is delivered. This behavioral selection (not a fixed pattern) will occur rapidly based on a species specific set of possible behavioral outcomes, and controlled by repeated switching (turn on or off) of those behavioral components to adapt the animal to the context at which maternal behavior is expressed (a nest, plus maze, reinforcement apparatus, presence of predator, stress, etc.). However, our view contrasts with the distinction of appetitive and consummatory behaviors commonly used in the area of motivation (as explained in detail in the next section) because it considers that passive and spontaneous behaviors or rapid behavioral switches (sometimes confused with reflexive or consummatory behaviors) can be highly motivated and goal directed and not show classical homeostatic properties assuming the existence of a drive that is satiated when the goal is reached.

3.2. Beyond appetitive and consummatory behaviors

A concept that is extensively used in motivational studies is the distinction between two sequential phases of a motivated behavior: an *appetitive* phase of flexible searching and instrumental responses performed to reach a desired goal, followed by a *consummatory* phase, consisting of stereotyped and species-specific behaviors that are initiated once the goal is achieved (Craig, 1918; Everitt et al., 2003). Based on this classification, Teitelbaum (1966, 1977) proposed that only flexible instrumental responses that can be modified by learning, and not those activated by reflexive mechanisms, should be considered motivated behaviors. Those flexible responses would reflect the willingness of the individual to obtain the goal. Accordingly, maternal behavior has been generally divided into an appetitive and a consummatory phase. For example, if a mother rat is separated from her pups, she first searches for the young (using pup ultrasonic vocalizations and olfactory information), and then generally picks them up, retrieves them to the nest site, licks and arranges them in the nest, and finally adopts a passive posture to nurse them (Stern, 1996). As discussed in Stolzenberg and Numan (2011), some authors consider that the searching phase (i.e. before reaching and picking the first pup), is the major appetitive component of maternal behavior while retrieving, licking, arranging the pups in the nest and nursing are consummatory behaviors elicited when the goal is achieved. However, others also consider retrieval or even licking as proactive and appetitive behaviors and only include nursing as the consummatory, and rather reflexive, response elicited after the animal has retrieved all the pups to the nest (Champagne et al., 2004; Numan and Woodside, 2010; Stolzenberg and Numan, 2011). The reason to consider retrieval as an appetitive behavior has been that retrieval behavior is performed by the mother to achieve the goal of returning pups to a safe nest where they can ultimately be nursed. That is a flexible, voluntary and active behavior that requires complex cognitive processing (such as remembering the site of the nest and choosing flexible routes to reach it, attention to avoid a possible predator, etc.). Besides retrieval behavior is also affected by experimental procedures that enhance or diminish maternal motivation (Afonso et al., 2007; Numan and Woodside, 2010; Pereira and Ferreira, 2006; Pereira and Morrell, 2011; Stolzenberg and Numan, 2011).

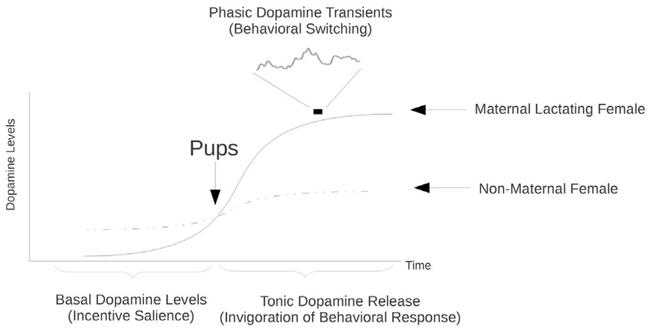

Fig. 2. Different hypothetical functions of NA DA dynamics in maternal motivation. Basal and tonic levels of DA in the NA increase salience and invigorate behavior, respectively. Transients, shown in the insert, would promote behavioral selection and switching.

These different views are a consequence of how consummatory behavior is defined: this term is sometimes used both for the activities performed when the goal is achieved and also for reflexive and stereotyped behaviors. For example, nursing postures are not necessarily reflexive, given that nursing postures can be maintained and adjusted by many factors independently of the presence of suckling stimulation. For example, suckling is not necessary for the newborn to stimulate nursing postures, also called crouching postures or behavior, in naïve (non-lactating) virgins of many species of rodents and primates. Therefore the assumption that maternal motivation has nursing as a final goal might not be appropriate from this perspective either. Maternal motivation persists, at least up to weaning, and does not necessarily satiate or extinguish after the animal interacts with the newborns (see next section). Retrieving newborns to the nest is a behavior that not only satisfies nursing, but also thermoregulation, social contact, and perhaps an urge to care as shown in rats by the common behavior of retrieving their own tail to the nest.

Although the definition of motivation and perhaps the origin itself of the word (*to move*) has influenced the type of research and predictions in the motivation field, the absence of an action (e.g. remaining with the pups in the nest), or immobility can also be considered a motivated behavior that includes inhibition of other active behaviors (for example escaping). Some of these passive (not consummatory) highly motivated behaviors include, for example, hiding (rather than escaping in a potential threatening situation), hovering over pups (thermoregulatory or protective function rather than nutritional as nursing), holding attention in a delayed reward (rather than continued work for it), or reading a baby-care book in humans (active sustained attention rather than motor activity). These behaviors are in fact, flexible, also voluntary, and require complex cognitive processes. The only difference is that passive behaviors, as revealed by the term, require less or no motor activity. Therefore, it might be more appropriate for the maternal motivation field to distinguish between active and passive motivated behaviors (only from the point of view of motor activity), rather than appetitive and consummatory behaviors. This view would also follow the original distinction of active and passive maternal components proposed by Terkel et al. (1979). Experiments could also be designed to test the intensity of these passive maternal

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

motivations; for example, by analyzing how much a mother avoids leaving the newborn and the nest area when confronted with a mild risk, or an alternative salient stimuli (food, sex, drugs). This paradigm of challenging the mother to leave the nest and the pups might be an interesting strategy to investigate passive components of maternal motivation, generally considered less appetitive (see also Section 5.3).

3.2.1. The satiation component of consummatory behaviors

Another problem with the distinction between appetitive and consummatory phases is the common association of the latter with satiation. The consummatory phase has been associated with alterations of the physiological state of the individual which, in turn, decrease the incentive value of the stimulus, thus impacting subsequent appetitive behaviors (Robbins and Everitt, 1996; Berridge, 2004). However, although this criterion fits well with the regulation of some of the motivated behavioral components of maternal behavior, for example nursing in some of the species and conditions discussed in our theoretical model (see Section 3.2.2), it does not hold for many other maternal behavioral components and conditions. Nursing, a behavior considered mainly consummatory, does not reduce the motivation (maternal *state*) of the mother rat, and the mothers of other altricial or semialtricial species, to remain in close proximity with the pups and adopt crouching postures for many hours. The female will continue adopting nursing postures even when the pups are full, showing no satiation of maternal motivation, in contrast to thirst, hunger or sexual motivational models (Agmo, 1999). Maternal animals keep retrieving pups until there are no more to retrieve, and they will commence retrievals if pups are removed from the nest and made available again at a distance (Wilsoncroft, 1969). Thus, the behavior of maternal females is different from that of a hungry or thirsty animal, which become satiated after food or water consumption, and is reinitiated once the animal is hungry or thirsty again, or for example when a highly palatable food is offered. Maternal animals will keep showing maternal behavioral components without the need of modifying the incentive value of the stimuli. Maternal motivation is a complex *state* that includes several behavioral motivated components that are maintained (with frequent switching among them) without a decline, for long periods of time, as long as the appropriate stimuli are provided (Bruce, 1961; Grosvenor and Mena, 1974). Besides, the continuing adaptation and capability of learning shown by mother rats tested for maternal behavior with changing stimuli (pups of different ages), environment conditions (elevated plus maze, preference test cages), and social contexts (presence or absence of intruders, or mating partners) is only made possible by a continuous high state of maternal motivation (maternal *state*) across the lactational period.

The need for a deprived goal (energizing effect) in order to search for it, and to reduce the drive, once the goal has been reached (satiation), are two concepts that have been the basis for most studies on behavioral motivation. These models of motivation are based on the concept that depriving the animals of the possibility to satisfy and satiate their internal needs (maternal *state* or drive), increases their motivation and the behaviors directed toward that goal-object (for revision see Berridge, 2004). For example, in conditional process such as place preference conditioning and operant procedures, an increase in proactive behaviors has been produced by the deprivation of a certain stimulus, such as newborn removal in lactating animals (Fleming et al., 1994; Lee et al., 1999). These manipulations can effectively increase the incentive value of stimuli and the proactive behaviors to obtain and care for the newborn. Maternal animals with high levels of motivation will actively seek and work in reinforcement paradigms to obtain newborns (Fleming et al., 1994; Lee et al., 1999; Mattson et al., 2001). However, as discussed previously, animals stop retrieving pups not because the motivation (maternal *state*) is satiated, but because their maternal *state*, once the goal has been reached (all pups have been retrieved), redirect them to lick, protect, and nurse the newborn (all maternal motivated behaviors). Deprivation of the reinforcing stimuli does affect motivational *states*, but only by increasing the probability of occurrence of the particular motivated behavioral components. Once those maternal behavioral components are performed the motivational *state* of the animal would not be satiated, only redirected to coordinate and organize the timing and frequency of the different maternal behavioral components. The contribution of deprivation/satiation theories is also limited in the sense that do not contribute to our understanding of the quick selection and activation/inactivation of motivated maternal behavioral components during mother–offspring interaction (e.g. licking vs. crouching vs. building a nest), or the quick selection and activation/inactivation of intrinsic motivational behavioral networks (to care for or reject; to desire or avoid) that results for example in spontaneous parental or infanticidal (i.e. pup killing) behavioral responses (see also Section 5.2).

3.2.2. The model of maternal motivation in 'intermittent' mothers

Although the diversity of parental responses shows that maternal motivational studies cannot universally use the appetitive vs. consummatory distinction, there are situations in which this distinction might be useful. In those species where crouching or retrieval does not occur (i.e. deer, rabbit), nursing might be more easily seen as a transient final goal that is actively searched for, and avoided when satiated. In many species with altricial or precocial offspring (i.e. rabbit, deer) mothers meet their infant for nursing for only a few times, or just once, a day (González-Mariscal et al., 1994, see also Olazábal et al., 2013). In the case of rabbits, the mother will nurse the offspring only after entering the nest (a behavior that can be considered appetitive and proactive), following a circadian periodicity (Jilge, 1993, 1995). In rabbits, nursing induces a refractory period during which the mother will not re-enter the nest box, even if new hungry litters are provided. The duration of such a refractory period is dependent on the number of suckling pups (González-Mariscal, 2007). However, this does not imply that rabbits and deer are not maternally motivated (in a maternal *state*) or are satiated but, rather, that the motivation to nurse (one of the behavioral components of maternal behavior) has been optimally adjusted by evolution to avoid the cost or risk of the mother and young staying together (risk of predation). Guarding behavior (also a motivated maternal component) is maintained during that refractory period. These types of adaptations to avoid predation of the young have probably played a critical role in the modalities of mother–offspring contact and interactions in these species.

In rabbit, those encounters end quickly and might be mediated by mechanisms similar to satiation, as seen in sexual behavior, but affecting only that particular maternal behavioral component. In rabbit and deer, the behavior appears to be induced, and temporally synchronized, by endogenous rhythms that regulate the timing of proactive seeking behavioral responses (enter or moving to the nest site in rabbits, or calling the hidden offspring in deer). However, this type of mother–offspring encounter requires a proactive and also synchonized motivated behavioral response from the young, that also vocalizes and approaches to the mother or nest. If the young rabbits were prevented from accessing the nest, the passive motivated maternal behavioral response of *waiting for the young* before leaving the nest again could also be investigated, as discussed at the end of Section 3.2.

In summary, differences in mother–offspring interaction in altricial, precocial and intermediate species, require different experimental paradigms and theoretical frameworks in order to understand maternal motivation in a comparative way. These substantial differences, far from limiting the studies of maternal

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

motivation, give us a great opportunity to investigate the neural basis of behavioral motivation with more complexity than has been done in the past (see also Olazábal et al., 2013). Our research has, so far, simplified this complexity by bridging concepts and paradigms between sexual and feeding motivational studies that might not properly apply to all maternal situations.

3.3. *Incentive motivation, liking and wanting*

Incentive theories of motivation have also guided most maternal motivation studies in the last decades and are still inspiring our work. These theories explain how approach or avoidance responses (e.g. how much the animal seeks or works to get pups or to avoid them) are elicited and guided by incentive stimuli (attractive or aversive), or their central representations, in interaction with central drive states (Berridge, 2006; Bindra, 1968, 1969). Newborns are strong incentive stimuli that acquire positive attractive value for postpartum animals and promote seeking behaviors toward them – *incentive motivation*.

Berridge and Robinson (1998) adopted the theory of incentive motivation and proposed that the process of reward can be dissociated into three separate components: a *wanting* component that represents the desire to obtain the reward; hedonic pleasure or *liking* which results from obtaining the reward; as well as reinforcement processes, where obtaining a reward results in *learning*. Although these components usually appear together, they reflect different aspects of a reward because they imply separate neuronal processes, and, therefore, can be separated under some circumstances or through experimental manipulations (Berridge, 2004, 2009; Smith et al., 2011).

Liking involves the processes underlying sensory pleasure triggered by an unconditioned or conditioned stimulus and can sometimes be measured objectively, for example by recording facial expressions generated by the impact produced by certain flavors in humans, monkeys, and also in rats and mice (Berridge, 2000; Steiner et al., 2001). This aspect of the response to rewarding stimuli is extremely difficult to study and it has been almost absent in the animal maternal behavior literature. The pleasent (hedonic) value of the pups for mothers has not been analyzed as a separate component from their incentive value. It could be argued that the licking of pups, due to its similarities with the *liking* reactions to sweet flavors, may be a good candidate for exploring the positive hedonic value of the pups for mothers. Also the amniotic fluids, that are avidly licked and consumed by parturient ewes (Lévy et al., 1983), and the placentophagia, displayed by parturient rats (Kristal, 1980) and rabbits (Melo and González-Mariscal, 2003) might indicate that such materials, not normally consumed by females, acquire a positive incentive value for them around parturition. In addition, nursing has also been considered as one of the most hedonic maternal activities that releases opioids and oxytocin (Machin and Dunbar, 2011; Nelson and Panksepp, 1998; Uvnäs-Moberg, 1998), but there are no studies specifically investigating or measuring liking reactions to suckling or ventral contact stimulation. Measuring only the liking reactions or expressions (excluding the wanting components) is extremely difficult in animals because liking reactions are commonly hidden for the observer. However, we think it is useful to continue thinking in creative ways to address this critical problem, as shown by Panksepp and colleagues (Burgdorfa et al., 2011; Harmon et al., 2008) in their elegant studies using 50 kHz vocalizations in rats as an indicator of positive affective states. Neural or physiological correlates of liking or positive affective states would be very useful and could complement these creative experimental designs. When thinking about this type of study, it is important to consider that the nature of the processes involved in liking or disliking can be unconscious or conscious (Berridge, 2009; Ikemoto and Panksepp, 1999), and animals can also experience different degrees of like or dislike, making the expressions or behavioral reactions of like or dislike more or less obvious.

On the other hand, *wanting* implies processes that assign incentive salience to a stimulus, that make it desirable independent of its hedonic value (Berridge, 2004). Salamone and Correa (2002) propose that this aspect of reward can be further subdivided into at least two components, one directional and another activational, related to the energizing aspects of motivation. This aspect of the rewarding value of the pups for mothers has been extensively studied in the rat and is described in detail later in this article (see Section 4). The incentive value of the pups modulates the execution of maternal behavior, and therefore it could be eventually studied directly through the detailed analysis of maternal caregiving responses toward pups (Stern and Keer, 1999; Pereira and Ferreira, 2006). However, by analyzing maternal motivation with this approach, explanations might become tautological, as it can be concluded that a rat is maternally motivated because the animal displays maternal motivated behaviors. One way to escape this circular reasoning has been to use instrumental, choice tests, or conditioned place preference paradigms. If a specific manipulation, like hormone administration, enhances the active components of maternal behavior, it can be predicted that non-maternal instrumental behaviors that bring the female in proximity with the pups will also increase. Through models designed to measure maternal motivation, it has been possible to assess the incentive value of pups with different characteristics (Pereira and Ferreira, 2006), or pups-related cues (Kinsley and Bridges, 1990) for lactating females. Also conditioned place preference procedures (Fleming et al., 1994; Mattson et al., 2001; Wansaw et al., 2008) and instrumental procedures, as bar pressing (Lee et al., 1999; Wilsoncroft, 1969), have been employed to determine the importance of hormones and experiences, among others, on maternal motivation. These experimental paradigms, do not discriminate the liking and wanting components, but have been very useful to study different motivated behaviors and its neural and neurochemical basis. We should also note in this type of analysis, that the reduction or the absence of work or effort to reach the goal indicates a reduced motivation in a specific challenging context, but it does not necessarily imply an absence of a maternal state and the performance of maternal behaviors in other, less stressful, challenging, or risky contexts. That is, a stimulus (a newborn, or a mating partner) can be liked and wanted (due to a maternal or sexual motivated *state*), but rejected under inappropriate conditions (risky situations such as a predator in vicinity). Two useful models to study maternal motivation in this new conceptual framework are described in Section 5.

4. Hormonal and dopaminergic mediation of maternal motivation

4.1. *Hormonal influences in maternal motivation*

New mother rats are attracted to pup-related stimuli even before parturition, mainly due to the hormonal profiles of the end of pregnancy (see Section 2). In particular, differences in E2:P4 ratio have been extensively investigated in relation to variability in maternal motivation (Numan et al., 2006, also see Section 2). Several studies in marmosets, rabbits, rats, and sheep show that higher E2/P4 ratio at the end of pregnancy increases maternal motivation (González-Mariscal and Rosenblatt, 1996; Numan et al., 2006; Poindron and Le Neindre, 1980; Pryce Ch et al., 1993). The influence of the gonadal hormones in strengthening maternal motivation is reflected in operant models in which mothers learn to press a bar to gain access to pup stimuli (Wilsoncroft, 1969; Lee et al., 1999), as well as in conditioned place preference models (Fleming

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

et al., 1994; Mattson et al., 2001). Thus, in parturient or hormonally treated mice and rats, the synergistic actions of E2 stimulation and P4 withdrawal, induces significantly more pup-reinforced lever presses (when pups are used as rewarding stimuli) compared to ovariectomized or intact virgins (Hauser and Gandelman, 1985; Lee et al., 1999).

Traditionally it has been assumed that the maternal behavior in non-primates is more dependent on gonadal hormone fluctuations than in primates (Keverne, 1996). However, in the past two decades, several studies in primates (including humans) have shown that hormones might also be related to maternal motivation and the quality of parental behavior, not only in females but also in males (Saltzman and Maestripieri, 2011). Human mothers at day 2 postpartum, who report feeling more, as opposed to less, attached to their new infant have a gestational profile of lower early pregnancy levels of E, and a relative increase in the ratio of E2:P4 as pregnancy advances (Fleming et al., 1997).

This relationship between E2 and P4 profiles has also been explored using operant paradigms in primates (Pryce Ch et al., 1993). Pryce Ch et al. (1993) have shown that pregnant common marmosets show more responses (bar pressing) to infant stimuli than virgins in an operant paradigm that uses visual (infant replicas) and auditory (played back vocalizations) stimuli. Moreover, they showed that the frequency of bar pressing and E2/P4 ratio were maximal just before birth, and that non-pregnant females treated to mimic changes in E2/P4 ratio at late-pregnancy exhibited increased operant maternal behavior (Pryce et al., 1993). As maternal motivation is less dependent on gonadal hormones during the postpartum period, (see Section 3), it is possible that the same neural systems that are modified by hormones at the end of pregnancy, are also activated and strengthened by newborns during the postpartum period in a hormonally independent way. The dopaminergic system appears to be one of those systems, and has been extensively studied.

4.2. Dopaminergic mediation of maternal motivation

4.2.1. Brief description of the theories on dopamine function in the nucleus accumbens

Before we review and discuss the role of dopamine (DA) in maternal motivation, we will briefly summarize the different theories on DA function in motivation and, in particular its actions in the nucleus accumbens (NA) (Groenewegen et al., 1996). DA action in the forebrain has been extensively studied (Berridge, 2006; Blackburn et al., 1992; Ikemoto and Panksepp, 1999; Kelly, 2004; Robbins and Everitt, 1996; Salamone and Correa, 2002; Schultz et al., 1997; Stolzenberg and Numan, 2011; Wolff, 2002) in relation to several behaviors (i.e. feeding, sexual, and maternal behavior), and experimental paradigms (i.e. bar pressing for reward, choice test, conditioned place preference, self stimulation). In particular, there is extensive evidence on the critical role of DA neurons in the ventral tegmental area (VTA) for the control of behavioral motivation. Specifically, VTA efferents to the NA, and its modulation of cortical, hippocampal, and amygdalar afferents to the NA has received much attention (Robbins and Everitt, 1996; Sesack and Grace, 2010). Although the goal of the present review is not to provide a detailed analysis of the different dopaminergic theories, we summarize a few main ideas that will aid in the discussion and interpretation of evidence that supports DA NA involvement in the regulation of maternal behavior.

There are at least six main functions or alternative theoretical interpretations (not exclusive) on the role of DA inputs to NA in behavioral motivation and reward processing. Initially, DA was associated with sensory pleasure or the experience behind a hedonic experience (Wise, 2008). Because there is strong evidence that the mesolimbic DA system also participates in negative emotional states and aversive motivations, as well as in the processing of novel salient stimuli, other alternative theories have also been proposed. Schultz et al. (1997), proposed that DA signaling was implicated in reward prediction, while Joseph et al. (2003), and Kalivas and Volkow (2005) supported a role for NA DA in associative learning processes, where salient stimuli would permit the formation of associations between them and more familiar stimuli in order to be used later in different adaptive situations. On the other hand, Redgrave et al. (1999), Sesack and Grace (2010), and Garris and Rebec (2002), emphasized the function of the DA system in attentional mechanisms, and the switching among different behavioral responses. According to this view, the main function of DA in the NA is to allow behavior to change in response to the situation or context at hand. DA, therefore, may play a role in behavioral selection rather than in reward prediction. DA response could assist in preparing the animal to deal with the unexpected by promoting the switching of attentional and behavioral resources towards biologically significant stimuli. Louilot et al. (1986), among others (Blackburn et al., 1992), have also visualized DA function in the NA as promoting flexibility and adaptation. Berridge and Robinson (1998, 2003), and Salamone and Correa (2002), consider that DA in the NA mediates incentive salience (wanting) processes, or the higher order motor or sensorimotor processes that are important for activational aspects of motivation, and response allocation respectively. Finally, Ikemoto and Panksepp (1999), proposed that the most important role of DA in the NA is to facilitate flexible approach responses by modulating incentive motivational processes, and the formation of incentive representations in the brain. According to these authors, NA DA transmission would play a critical role in invigorating flexible approach responses when organisms encounter salient stimuli (incentive and novel stimuli). Both avoidance and appetitive behaviors may share the arousal of an approach-seeking system in order to promote life-sustaining states of affairs. Currently, there is extensive research supporting each of the different theories summarized above. We will next review the contribution of maternal behavior studies to our understanding of DA function in the NA to see which theory best explain our data and our conceptual framework.

4.2.2. Manipulations of the dopaminerigc system and maternal motivation

Several studies found that DA antagonists induce a deficit in retrieval behavior (proactive component of maternal behavior) in maternal rats and voles (Giordano et al., 1990; Stern and Taylor, 1991; Fleming et al., 1994; Stern and Keer, 1999; Byrnes et al., 2002; Lonstein, 2002; Pereira and Ferreira, 2006; Zhao and Li, 2010). Strong evidence suggests that activation of the mesolimbic DA system is essential for the occurrence of maternal behavior (see Numan and Stolzenberg, 2009; Numan and Insel, 2003). In early studies, Hansen et al. (1991a,b) found that 6-OHDA lesions in the ventral striatum produced deficits in retrieval behavior but not in nursing, an effect that could be overcome by increasing the motivation of the mother with a short period (4–6 h) of separation from the pups. Similarly, Keer and Stern (1999) found deficits in retrieval behavior with DA antagonist infusions into the NA. More recently, Numan et al. (2005a) found that DA antagonists of D1 receptors in the NA specifically induced a deficit in retrieval behavior, while D1 agonists reduced the latency to induce maternal behavior in pregnancy terminated naïve female rats (Stolzenberg et al., 2007). All these studies support the idea that DA in the NA is necessary for the proactive components of maternal motivation (retrieval and in some cases licking was affected). Nursing has consistently not been affected (sometimes even facilitated) by either systemic or intra-NA infusions of DA antagonists or DA depletions in the NA.

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

4.2.3. In vivo monitoring of dopamine in maternal animals

Up until the last decade, there were very few studies (Hansen et al., 1993; Kendrick et al., 1992) that had used microdialysis or voltammetry techniques to study the dynamics of DA release in the brain of maternal animals. Hansen et al. (1993) were the first to demonstrate increased dopaminergic activity in the ventral striatum of mother rats when they were reunited with their newborns after an overnight separation. They found that when the pups were dirty (soiled with earth), DA activity increased still more. However, this increase was associated with more nest building, retrieval, grooming and digging (all active maternal and non-maternal responses), but there was less licking/sniffing and similar or reduced nursing during that time.

In a recent series of studies, Fleming and her colleagues have produced the most detailed evidence on the role of tonic DA in the NA (extrasynaptic basal or stimulated DA release that has a slow time course). In these studies the authors provided evidence on the relationship between DA and (1) hormonal profiles associated with late-pregnancy and parturition, (2) prior maternal experiences, and (3) salience of pup stimulation.

4.2.3.1. Dopamine and hormones. When provided with rat pups, postpartum females show large and sustained elevations in DA in the NA. These elevations occur against a background of a hormonally mediated suppression in basal tonic DA release (Afonso et al., 2009). In the absence of any prior pup-experience, ovariectomized rats treated with P4 and E2 (which induces maternal responsiveness to foster pups), display a similar reduction in basal DA responses as postpartum intact mothers, and a similar initial increase in response to pup presentation (Afonso et al., 2009). The more rapidly a rat becomes maternal under the influence of hormones, the lower basal DA prior to pup exposure. Thus, hormones that facilitate maternal responsiveness in the absence of previous maternal experience have the same effects on NA DA functioning as in the intact postpartum experienced female, and this hormone-induced basal suppression is related to heightened maternal responsiveness.

4.2.3.2. Dopamine and maternal experience. Compared to cycling but previously experienced female rats, cycling pup-naive rats do not display suppressed basal DA, and also do not show a DA response to pups. While these data might suggest that the DA response to pups is dependent on a reduced baseline, this conclusion is not warranted. Cycling females, who have had prior maternal experience after an earlier pregnancy do not show a reduced baseline DA, but they do show a rise in DA with presentation of pups (Afonso et al., 2008).

Prior experience with pups affects the DA response to subsequent pup exposure. In fact, there are additive effects of maternal experiences. Multiparous females that are re-induced to be maternal through constant exposure to pups immediately prior to maternal testing show a greater pup-evoked DA responses than multiparous females with no recent pup exposure, or virgin pup-sensitized females (Afonso et al., 2008). All three experienced groups show greater pup-induced DA responses compared to virgin pup-naïve females (Afonso et al., 2008).

In summary, these studies suggest that the hormonally induced reduction of basal DA transmission in the NA is related to the rapid expression of maternal behavior in the postpartum rat. The females that demonstrate robust DA responses to pups also have a robust suppression in basal DA release. It can be argued that basal DA suppression aids the rapid expression of maternal behavior through a reduction in the DA noise in the absence of other stimuli. In this way, it might serve as a mechanism for sharpening the DA signal in response to pup stimuli and augmenting the primary pup-experience such that saliency develops. Impairments to basal suppression (e.g. by manipulations of the early environment, Afonso et al., 2011), would be expected to result in a consequent DA signal decrease and a reduction in pup salience, culminating in impaired mother–pup interaction.

4.2.3.3. Dopamine and stimulus specificity. Does this signal-to-noise mechanism result in sharpened DA signals to all stimuli, or only to pup stimuli, in postpartum females? In subsequent studies Afonso et al. (2009, 2013) compared the behavioral and DA profiles of female rats when exposed to (1) pups and (2) palatable food (sweet cereal). Both nulliparous and parous females showed increased DA responses when ingesting the sweet treat. However, only postpartum females showed pup-evoked DA responses greater than the food-evoked DA responses; a finding not observed in cycling females even after pup-experience. The enhanced DA responsiveness to pups in postpartum females is sustained even when the dams are exposed to pups in a perforated box at a distance and cannot interact with them (Afonso et al., 2013).

In summary, these recent microdialysis studies suggest that with maternal suppressed basal DA in the NA, pups take on robust saliency to hormonally primed or postpartum females. This is reflected in significantly increased pup-evoked DA release, even in the absence of actual interactions with the pups. In the absence of the hormones of parturition, DA release also occurs in response to pups in maternal animals but not in non-maternal animals; however this elevation is not preceded by a reduction in baseline characteristic of the hormonally primed animal and is sustained for less long. There is, nevertheless an additive effect of maternal experience on DA release. DA in the NA therefore likely mediates pup salience brought about through exposure to hormones or to sustained pup exposure and thereby contributes to the expression of maternal behavior.

Pereira et al. (2011) have also found a robust increase in NA core DA release associated with pup-seeking behavior (presentation of pups behind a screen). Such DA release was further augmented significantly during active (but not passive) maternal interaction with pups. Interestingly, although the pattern of DA release in relation to maternal behavior was similar in late postpartum females, the magnitude of release was considerably attenuated in late compared to early postpartum females behaving maternally (Pereira et al., 2011).

DA transients (spike-dependent fast increases in DA, Grace, 1995) during mother–offspring interaction have also begun to be investigated using in vivo voltammetry. Champagne et al. (2004) found increased DA signal in the NA in mothers that showed heightened licking and grooming of their newborns; however, the onset of the DA signal preceded the behavior. DA transients were also analyzed by Robinson et al. (2011) during pup investigation, and inmediately before or during retrieval. The major transient DA signaling was found while the mother was investigating the cage and newborns previous to retrieving them, and during the first retrieval; subsequent retrievals were not associated with DA transients. Thus, Robinson et al. (2011) proposed that DA transients might play a role in switching behaviors (maternal or not). However, as the authors also suggest in their study, careful series of studies in a more naturalistic environment could significantly contribute to our understanding of the role of DA transients in the NA prior to and during mother–offspring interaction, and in the transitions among the different behavioral components (retrieving, licking, nest building, hovering over the pups, and nursing). It might also be interesting to determine if those transients of DA change across lactation.

Considering that lactating mothers spend most of the time nursing, which requires a reduction in locomotor activity, lower basal tonic DA release in the NA during nursing in postpartum females would also fit with the evidence supporting an association between

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

high tonic levels of DA and increased locomotor activity and the active components of maternal behavior. Besides, following Ikemoto and Panksepp view (1999), and given the role of NA DA in behavioral invigoration, low, moderate and high increases in tonic extracellular release of NA DA in nulliparous non-sensitized, nulliparous sensitized/multiparous non-sensitized, and multiparous sensitized/postpartum females in the studies of Afonso et al. (2008, 2009, 2011, 2013) may be, respectively associated with the animal experiences of curiosity, interest, and urge. As discussed previously there are different intensities of motivation, and wanting that might be signaled in part by DA release.

It is also interesting to note that, despite the fact that DA release in the NA has been associated with the processing of aversive stimuli (measured both by in vivo microdialysis and voltametry, Blackburn et al., 1992; Ikemoto and Panksepp, 1999; Joseph et al., 2003), naïve cycling females exposed to newborns did not show any change in DA levels (Afonso et al., 2008, 2009, 2011). Although female rats have been described as neophobic toward newborns, important variability in the intensity of aversion to newborns has also been reported in the laboratory rat (Jakubowski and Terkel, 1985). Thus, it is possible that naïve females in Afonso et al.' studies (2008, 2009, 2011) showed a passive or neglecting behavioral response toward newborns rather and an active avoidance or highly invigorating behavioral response of rejection something that, for example, is more common in mice (infanticidal responses, Kuroda et al., 2011), and sheep (head hits and pushes, Nowak et al., 2011). So far, it is not known if DA is released in the NA in animals that show a strong aversion or rejection toward the newborns (see also Section 5).

4.2.4. Dopamine action in other brain regions related to maternal motivation

DA release into the NA in maternal animals would be promoted mostly by inputs from the medial preoptic area (mPOA) to the VTA as proposed by Numan (2006) and Numan and Stolzenberg (2009) (see also Olazábal et al., 2013). The mPOA, under the action of the hormones at the end of pregnancy, would activate VTA DA neurons that would then release DA into the NA (see Fig. 3). The model of Numan and collaborators (Numan et al., 2005b; Numan and Stolzenberg, 2009) proposes that the mPOA stimulates VTA DA input to NA to *suppress* NA GABAergic inhibitory input to the ventral pallidum (VP). Such a disinhibition of VP allows VP efferents to promote active maternal responses. In addition, the NA and the VP, through its projections back to the mPOA, or via VP-medial thalamus-prefrontal cortex-NA can also adjust the ongoing behavioral performance (Fig. 3).

However, DA is released not only into the NA, but also into the medial prefrontal cortex (mPFC), dorsal striatum, hippocampus, amygdala, and septum, among other regions (Kalivas and Volkow, 2005; Kelly, 2004; Wolff, 2002). Although the mPOA-VTA-NA circuitry has been studied extensively, the mPFC-NA influences, or modulation of the mPOA-VTA-NA network by the mPFC has attracted less interest. Cortical inputs have a major role in the control of ongoing maternal behavior, maternal adaptations across postparutm, the switching among different motivated behaviors, or the selection of an appropriate behavioral response, particularly in situations where new contextual environmental information needs to be added and novel response strategies chosen (see Section 5.3, Afonso et al., 2007; Pereira and Morrell, 2011; Olazábal et al., 2013). Therefore, it is intriguing to know how tonic and phasic dopaminergic activity in the mPFC is expressed in postpartum females, and especially, at the postpartum estrus, when new mothers are confronted with newborns, males, or both stimuli (see Section 5.3). As well, it is of interest to know what is the role of the PFC glutamatergic inputs to the NA, which modulate DA activity in the NA (Blackburn et al., 1992).

Afonso et al. (2007) recently found that lesions of the mPFC disrupted the frequency, duration, and execution of many maternal behavior sequences that require the coordination of sensory and motor information in a spatial context (e.g. retrieval behavior and licking). The VTA also sends projections to the PFC, basolateral amygdala (BLA) and septal/hippocampal areas. In this way maternal behavior can be adjusted and organized by hippocampal, PFC, and amygdalar inputs to the NA, modulated by DA. Pereira and Morrell (2011) confirmed and extended those results reported earlier after global lesion or inactivation of mPFC (Afonso et al., 2007; Febo et al., 2010), by demonstrating a critical role for the infralimbic (IL) subregion of mPFC in early postpartum maternal behavior. Pereira and Morrell (2011) data also show that, with the progression of the postpartum period, the necessary facilitatory role of the IL subregion wanes, and other mPFC subregions, such as the prelimbic (PrL), are recruited to maintain late postpartum maternal behaviour (Pereira and Morrell, 2011; see also Olazábal et al., 2013). The importance of the mPFC in mothers planning, and cognitive flexibility has also been studied, and is still more obvious in humans, and will be reviewed in more detail in Olazábal et al. (2013).

Putting together the findings of Hansen et al. (1991a,b), Afonso et al. (2008, 2009, 2011, 2013), Champagne et al. (2004), Robinson et al. (2011), and the current knowledge of the cortical modulation of DA tonic levels in the NA (Grace, 1995; Parker et al., 2010; Blackburn et al., 1992), we can speculate that maternal experience and hormonal priming modifies DA modulation of mPFC-NA input as suggested in Sesack and Grace (2010), through a reduction in tonic DA in the NA. As proposed by Blackbrun (1992), DA would serve to enhance the signal-to-noise ratio of sensory stimuli. Thus, the reduction in the basal tonic DA in postpartum females, together with the slow and sustained rise of DA when exposed to pups, and the DA transients found during mother–offspring interaction and behavioral transitions, might respectively increase pup salience, invigorate the female to approach to them (maternal motivated *state*), and then provide a mechanism to facilitate selection and switching among the different maternal and non-maternal responses appropriate to the context of the test (Fig. 2). A regional increase in corticostriatal activity might also increase tonic DA release in the NA (Grace, 1995; Parker et al., 2010), thus blunting the phasic DA response in this structure. This might be a mechanism by which control or switching between different motivations or the attention to the different stimuli can occur. In summary, our interpretation of DA NA function support the theories proposed by Berridge and Robinson (2003), Blackburn et al. (1992), Ikemoto and Panksepp (1999), Redgrave et al. (1999), Sesack and Grace (2010) and others, assigning to DA NA several roles in the mediation of incentive salience (wanting), invigorating flexible approach responses, and switching among different behavioral responses. Specific studies designed to test the role of DA NA in maternal learning are scarce (except D'cunha et al., 2011; Parada et al., 2008). DA NA might be important to associate stimuli or switch attention and prepare the animals to learn about particular contexts at which newborns are presented. However, we think it is unlikely that DA transients predict newborn appearance (as in the error predictor hypothesis of Schultz et al., 1997) as suggested by Robinson et al. (2011) because their animals clearly show DA transient after pups are already in the cage and they are engaged in exploratory activities away from the pups. However, the error predictor hypothesis of Schultz et al. (1997) deserves experiments specifically designed to test it. In addition, the presence of high levels of crouching and nursing in DA depleted animals, and the association between DA tonic levels and transients with active maternal components and anticipatory activities/behavioral selection respectively, do not support the idea that DA in the NA mediates liking or 'pleasurable' experiences. The role of excitatory inputs to the NA, as well as the

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

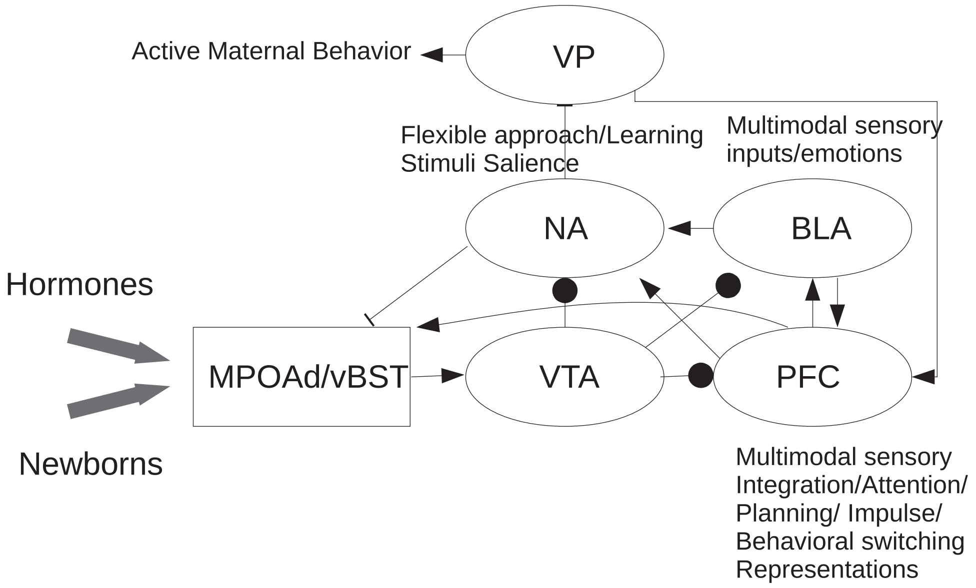

Fig. 3. The figure shows a hypothetical model for explaining the stimulation of active components of maternal behavior and its modulation by cortical areas and the mesolimbic system. The action of hormones at the end of pregnancy and the prescence of newborns stimulate MPOA/vBST projection to the VTA that provokes the release of DA in the NA, PFC and BLA. DA release in the NA inhibit VP output promoting the active components of maternal behavior. The NA, VP, PFC and BLA can modulate that pathway by its connection to the MPOA/vBST or NA. BLA (basolateral amygdala), vBST (ventral part of the bed nucleus of the stria terminalis), MPOA (the medial preoptic area), NA (nucleus accumbens), PFC (prefrontal cortex), VP (ventral pallidum), VTA (ventral tegmental area). Lines ending in arrow, circle, or vertical bar signify excitatory, dopaminergic, and gabaergic projections respectively.

participation of other NA neurotransmitters and peptidergic systems (e.g. opioids, orexins, oxytocin) in these active and passive maternal behavioral responses, and wanting/liking components of maternal motivation need to be investigated in more detail.

5. Specificity of motivational systems

5.1. *Coordination of multiple specific and unspecific motivational systems*

Different specific and nonspecific motivational systems coexist and are used by individuals to explore the environment, and to adapt to the different challenging situations encountered in their lives. Therefore, animals need first the existence of certain intrinsic motivational systems, not necessarily to reach a specific goal, but rather to satisfy a certain curiosity to learn from their environment, to develop an interest in different aspects of it, and to make use of the resources it provides. During this exploratory activity animals would interact with different stimuli and respond according to their biological value. Therefore, both specific and unspecific motivational systems should coexist and be coordinated optimally.

Animals generally show the flexibility to adapt their behavior rapidly to satisfy different motivations and to perform optimally in a given situation/environment. A disadvantageous context can make an animal quickly abandon, kill, transport, or protect the newborn from predators. Mothers are also able to take care of the newborn, at the same time that they accept partners to mate immediately after parturition (postpartum estrus, see Agrati et al., 2008, 2011; Connor and Davis, 1980; Gilbert et al., 1984; González-Mariscal et al., 2009). Therefore, maternal animals do not act according to fixed patterns but, rather, make decisions quickly based on contextual information, emotional and internal states (including multiple motivations). These rapid and contextual responses may also occur within seconds (spontaneously) and can be triggered by the properties of the stimuli without major changes or modifications to the general arousal or motivational *state* of the individual. An animal might direct or redirect, rather than increase or decrease, a basal arousal state towards a different set of stimuli or goals, as probably occurs in normal exploratory activity (see Section 3). Similarly, animals can suddenly stop performing a motivated behavior while they assess the risk or the advantage of maintaining a certain behavioral response without changes in arousal or motivational *state*. For example they might be aroused to act, but redirect that arousal when a risky situation is encountered, as is proposed to occur in displacement behavioral activities. How the brain can coordinate two simultaneous motivations, as when mothers escape from their homecage carrying a newborn in their mouth; or when mothers alternate between sexual behavior and maternal aggression in their homecage? What does this conceptualization about competing motivations and their coordination tell us about the control of motivation? In the laboratory, usually one motivation is studied at a time to simplify the experimental conditions. However analyzing how co-activated motivational systems interact may allow a deeper and more complex understanding of the neural bases of animal behavior in real life. How the maternal brain coordinates unspecific and different specific motivations is part of what we are trying to understand and will discuss some examples in the following sections.

5.2. *Spontaneously parental and infanticidal motivation*

Spontaneously parental or infanticidal animals direct their attention and arousal to take care or attack the newborns in a flexible, rapid, and oriented manner. Although ‘spontaneous’ parental or infanticidal responses are motivated rather than reflexive, these behaviors present several particular challenges and opportunities. In mice, Hauser and Gandelman (1985) found that virgin sensitized female mice work (bar press) to take care of pups, but it is unknown if male mice (typically pup killers) would work to kill the pups, showing then a proactive negative motivated approach. The onset of those maternal or killing motivational states is very rapid and can be modulated (e.g. delayed) pharmacologically (Neckers et al., 1975). Most adult prairie voles are attracted to pups immediately, but around 10–20% will attack the pups. These infanticidal females might continue attacking pups even after repeated exposure suggesting that those behavioral responses are highly motivated. Spontaneous parental or infanticidal responses in prairie voles are based on immediate decisions, likely influenced by previous life experiences that affected their affective state, their behavioral control, or the perception of pups. In the case of female prairie voles, this previous affective state (e.g. anxiety, increased aggressiveness) appears to make most animals to continue killing the pups 2 months later and after experiencing postpartum maternal behavior (Olazábal, 2010). As discussed in Section 3, these spontaneous maternal or infanticidal responses do not require previous parental or infanticidal experience or deprivation in order for the behavior to be expressed, and in many cases animals will also care for, or attack newborns as long as the young are presented, without an obvious inmediate satiation (Olazábal, 2010). However, this is not always the case. It is intriguing that some naïve female prairie voles (Olazábal personal observation) and postpartum female mice (Vandenbergh, 1973) can eventually kill a pup and take care of the others. This is also valid for human cases of infanticidal behavior (Rougé-Maillart et al., 2005). That is, killing of a newborn or infant does not necesarily include their siblings, and can be the consequence of a context or transient affective/emotional dependent selection of an inappropriate behavioral outcome. A motivated behavior like this can have wanting but disliking components. This takes us to one of the main points of this review, the distinction between a motivational *state* and the motivated behavioral components selected under that *state* (maternal or not), or the quick switch or coexpression of two opposite motivated behaviors.

Experiments designed to transiently challenge the motivation of the animal to have access to a pup or to keep a pup can be useful in order to understand maternal motivation and the mechanisms underlying the transient interruption, or activation of competing behavioral responses (pup killing). Stress or risk assesment can inhibit a motivated behavior completely or transiently, stopping or delaying the display of a certain behavior until the threatening or stressful situation disappears. Under those situations animals must show flexibility and the capacity to switch and control different types of motivations. Because spontaneous or rapid behavioral responses require rapid processing and decision making, these challenging experimental paradigms can be useful to investigate those processes (see also the next section).

5.3. *Maternal and sexual motivation at the postpartum estrous*

An excellent model for studying the co-existence of competitive social motivations is the postpartum estrous (PPE) in the rat, as females have a fertile estrus generally the night following delivery, during which they are both maternally and sexually motivated (Connor and Davis, 1980; Gilbert et al., 1980, 1984). In contrast to the positive value that a male has for a sexually active female (Bermant and Westbrook, 1966; Paredes and Alonso, 1997), a male intruder in the home cage of a postpartum female is highly aversive, often evoking vigorous attacks from the mothers (Erskine et al., 1978; Ferreira and Hansen, 1986). Therefore, sexual solicitation and maternal aggression can be considered mutually exclusive behaviors (Lin et al., 2011).

Interestingly, in the physiological context of the PPE, postpartum females tested in their home cage exhibit a combination of sexual and maternal aggressive responses toward a male. Moreover, the concurrent expression of these behaviors is as intense as their single expression, indicating that females can co-express sexual and maternal aggressive motivations in a short temporal window (Agrati et al., 2011). This study also reveals that the same stimulus, a male, can acquire a double affective valence (positive and negative emotion), indicating that positive and negative valences are not necessarily exclusive. This last assumption leads to a theoretical quandary (Colombetti, 2005): can positive and negative valences coexist?

The behavior of the PPE mother rat in her homecage is oriented mainly toward the male, courting and attacking it at the same time (Agrati et al., 2011). However, when given the choice between the pups and a male in a preference test, she ignores the male (Agrati et al., 2008), and courts – without aggression – when able to copulate far away from the nest (Gilbert et al., 1980, 1984). Taken together these studies stress the importance of the context in determining the behavioral outcome when two incentive stimuli are present at the same time. Thus, the motivational value of the male and the pups for the PPE mother rat, not only influence one another, but also change depending on the situation. This capacity of the mothers to express multiple motivations and to flexibly evaluate and assign affective values to stimuli according to the context enriches their behavior and allows them to display contingent responses to the pups and the environment.

What represents the ambivalent behavior of PPE rats towards the male in terms of neural processing? According to motivational theories stating that the interference between two co-activated motivations is due to the limitation of attentional resources (Afonso et al., 2007), the rapid shifts between sexual solicitations and attacks may represent the concurrent parallel processing of two equally high and opposite motivations that alternate because of attention shifts between the male's attractive and aversive attributes. Along this line, lesions of the mPFC, an area involved in attentional selection, and task switching (Afonso et al., 2007), affects particularly the more complex and interactive sexual and maternal responses of the female rats, sexual solicitation towards the male, and pup retrieval (Afonso et al., 2007; Pereira and Morrell, 2011).

Alternatively, it has been proposed that ambivalent emotions may emerge from simultaneously attending to positive and negative features of a single stimulus (Cacioppo et al., 1997, 1999; Norris et al., 2010). The integrated expression of sexual behavior and maternal aggression may indicate that the PPE mother rat perceives the male as attractive and aversive simultaneously, coupling both affective values in integrated motivational circuits. Is maternal aggression against a male during the postpartum estrus a wanting/disliking, wanting/liking, active avoidance/disliking, or active avoidance/liking combination of experiences? (see Section 3.3). Accordingly, Reynolds and Berridge (2008) found that appetitive, aversive, and a mix of appetitive and aversive motivated behaviors, can be generated by stimulating or inhibiting specific microcircuits in the shell region of the NA. Interestingly, this neuroanatomical map of motivated/affective behaviors is shaped by the environment, as for example, a stressful context expands the stimulation zones that evoke ambivalent behaviors (Reynolds and Berridge, 2008). Further studies are needed to understand the neural basis of the expression of more than one motivation when they are co-activated, and the PPE female gives us a promising opportunity to reach this goal.

6. The specificity of mPOA neural circuits that regulate the proactive components of maternal behavior

We have briefly reviewed the evidence for the role of the mPOA and its neural connections in the regulation of maternal motivation (see Numan, 2006, and Numan and Stolzenberg, 2009): mPOA projections to the VTA, which allow the mPOA to interact with the mesolimbic DA system so that DA is released into the NA, influence what has been generally considered the appetitive or proactive aspects of maternal behavior in rats, such as pup-seeking behaviors and the retrieval response. Numan (2006) referred to this functional neural connection as an interaction between a *specific* maternal

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

motivational system (mPOA) and a nonspecific motivational system that regulates an organism's responsiveness to a wide variety of biologically significant stimuli (mesolimbic DA system).

An important question to resolve, however, is whether there are mPOA neural circuits that are in fact specific for the proactive components of maternal behavior. In a recent review, Stolzenberg and Numan (2011) summarized the evidence that the mPOA is also involved in the proactive aspects of male sexual behavior and female sexual behavior in rats: Fos expression is displayed in the mPOA during each of these behaviors, and depression of mPOA activity disrupts the proactive aspects of each of these basic reproductive behaviors. Stolzenberg and Numan (2011) suggested that mPOA projections to the VTA might influence the motivation to engage in each of these behaviors, although the evidence favoring this perspective was greatest for maternal behavior, and more definitive evidence will be needed to support that proposal with respect to male and female sexual behavior.

It is in this context that the issue of the specificity of the mPOA, and its connections with the mesolimbic DA system, for maternal motivation arises. For example, during the postpartum, a female exhibits high maternal and sexual motivation. What is the specificity of mPOA involvement? Newman (1999) has argued for the existence of a social behavior network, where an integrated group of hypothalamic and limbic nuclei regulate a variety of social behaviors, such as maternal behavior, sexual behaviors, and aggressive encounters. Although a similar group of brain nuclei may regulate a variety of social behaviors, the important issue is whether the same population of neurons within this network regulates all the basic social behaviors, or whether there are distinct populations of neurons intermingled within the overall network, each of which is selectively involved in a particular social behavior. Although current research, particularly with respect to the mPOA, has not settled this issue, our bias is toward a labeled-line point of view, with distinct mPOA neurons regulating the proactive aspects either of maternal behavior, male sexual behavior, or female sexual behavior. This perspective does not mean that these microcircuits do not interact, but it does suggest that specific mPOA neurons stimulate the proactive aspects of a single social behavior.

As indicated, there is good evidence that mPOA projections to VTA control maternal motivation, but more evidence is needed with respect to male and female sexual motivation. Recent methodological advances have become available so that this issue can be more definitively investigated. Optogenetic techniques (Yizhar et al., 2011) can allow investigators to either directly excite or inhibit mPOA projections to VTA neurons, using photostimulation of mPOA axon terminals via implanted fiber optic wires. If it could be shown that stimulation of mPOA to VTA projections increases, and inhibition of these projections depresses, the proactive components (also called appetitive) of all three reproductive behaviors, then a very good case could be made that mPOA interactions with VTA neurons regulate all three major classes of reproductive motivation. Advanced optogenetic procedures can even allow one to selectively affect those mPOA neurons that are part of an mPOA to VTA to NA circuit (see Yizhar et al., 2011).

If it could be proven that mPOA projections to VTA influence all three reproductive behaviors, the next question is whether the same or different mPOA neurons are involved. One view, which we will call the common population view, would propose that the same population of mPOA neurons projects to the VTA to influence male sexual behavior, female sexual behavior, and maternal behavior. If that were the case, what kind of process would determine motivational and behavioral specificity? For example, although a lactating female on day 1 postpartum responds positively to both pup stimuli and sexually active males, a lactating female rat on day 5 postpartum, that is not longer in postpartum estrus, shows strong maternal behavior, but is not interested in mating with males. The common population view might argue that the particular hormonal milieu that mPOA neurons and other brain regions are exposed to regulates the particular stimuli that are able to activate the common mPOA neuron population that projects to VTA. That is, for the day 5 lactating female, only pup stimuli activate this common mPOA pool, while for females on day 1 postpartum, during the postpartum estrus period, both pup stimuli and male stimuli would be able to activate this common mPOA pool. In contrast, a labeled-line point of view would argue that separate populations of mPOA neurons that project to VTA are activated by either pup stimuli or male stimuli.

Fos is expressed in the mPOA during maternal behavior (Mattson and Morrell, 2005; Stack et al., 2002) and female sexual behavior (Coria-Avila and Pfaus, 2007). Recent anatomical methods are now available to allow us to determine whether such Fos is expressed in the same or different mPOA neurons. Based on work on aggressive behavior by Lin et al. (2011), one could employ a method referred to as cellular compartment analysis of temporal activity by fluorescent in situ hybridization (catFISH) to compare c-Fos expression induced during two consecutive behavioral bouts in a single animal. Immediately after engaging in a particular behavior, cfos mRNA is expressed mainly in the nucleus of cells, while 35 min later it is expressed in the cytoplasm where translation occurs. Using this method, one could perform the following experiment. At the postpartum estrus when both maternal and sexual behavior can be expressed, first allow females to interact and mate with a male for 5 min. Thirty minutes later, let the females interact with pups for 5 min and then sacrifice the females and process their brains with the catFISH method. If separate populations of mPOA neurons are involved in each behavior, then some mPOA neurons should show nuclear cfos mRNA fluorescence ('maternal neurons'), while a separate population should show cytoplasmic fluorescence ('sexual neurons'). If the same population of mPOA neurons regulates both behaviors, then most mPOA neurons should show both nuclear and cytoplasmic fluorescence. See Lin et al. (2011) for additional methodological information.

How the brain controls motivational specificity is an important question that warrants further investigation. Future research will allow us to determine whether specific mPOA neurons are involved in specific motivational states, or whether the mPOA plays a more general and nonspecific role in reproductive motivation, with the specificity of each behavior being determined by distinct mechanisms (differences in neurotransmitters, neuropeptides release, receptors expression; synaptic anatomical changes, etc.) that do not require the participation of distinct mPOA neurons. This is, therefore, a similar question to that proposed by Lin et al. (2011) and Veening et al. (2005) for the control of aggression and sexual behavior, or by Pennartz et al. (1994) on the activation of particular ensembles of the NA to activate one or other motivational system. The evidence so far suggests that there are subsets of neurons within a brain region that activate specifically one or another behavior, while others neurons play a more general role. How this result in coordination or coexpression of two different opposite behaviors is still unknown. However, it can be hypothesized that the alternation or coexpression (when physically possible) of sexual and maternal behavior or proceptive behaviors and attacks (maternal aggression) in PPE mother exposed to newborns and a male, can occur by the planning and organization of the behavioral output by the PFC and different subset of neurons in the mPOA-VTA-NA-VP path.

7. Conclusions and perspective

We believe that future studies on maternal motivation will continue adding complexity to the system, and contribute to our understanding of the mechanisms that regulate the selection and

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

regulation of behaviors, and the nature of processes underlying maladaptive behaviors and psychopathologies. Below, we summarize the main advantageous features of these studies and the challenges we are currently facing.

First, we consider that some classical concepts in the field of behavioral motivation need to be revised and clarified in order to add complexity to the behavioral analysis, and to our experimental designs. In this review we show that most of our studies have really focused on distinguishing the neural bases of proactive motor vs. passive components of maternal motivation. This distinction does not necessarily fit with the classical distinction of appetitive and consummatory behaviors because, in many cases, the distinction represents a crude simplification of the complexity of the behavioral processes underlying maternal motivation. In the past, in order to develop good tools to measure maternal motivation and determine its neural basis, fundamental aspects of behavioral motivation have been simplified. In particular, maternal motivation is a *state* that is maintained for long periods of time (without satiation) with continuous alternation of proactive and passive behavioral responses equally relevant for the mother and for the survival of the offspring. We consider that paying more attention to passive (but not consummatory, as discussed in this review) motivational features of maternal behavior will add significantly to our understanding of maternal motivation. It can also uncover the neural mechanisms that maintain contact with the stimulus or transiently turn off that contact or interaction. Studying the mechanisms that maintain maternal motivation across or even beyond lactation in many species can also be seen as a challenge for the future.

Another point that we highlight in this review is the need to investigate the specificity of motivational systems and the coordination among them. Using the example of the multiple behavioral motivations that are present, for example, in the female rat at the postpartum estrous or in spontaneously maternal or infanticidal rodents, we raised three large questions. One is the neural basis of rapid switching between different motivational systems, and the coexpression of multiple motivations in a flexible new, unique and contextual series of behavioral events. The second question focused on the role of DA release in the NA in the mediation of maternal vs. other motivations. We propose a role for DA release in the NA in generating interest, increasing salience of stimuli, promoting invigorating proactive behaviors, and facilitating the switching between maternal and non-maternal behavioral responses.

The last question asks how subsets of neurons in a brain region that participates in two behavioral responses and motivations might be organized to regulate both simultaneously. We discuss evidence on two alternative but not mutually exclusive hypotheses. One hypothesis is that the same neurons in different brain regions are activated simultaneously, but by different stimuli (sensory or hormonal), or with differents pattern of activity, generating different behavioral responses (for example sexual vs. maternal behavior). A second hypothesis, that seems to be supported more strongly by the evidence, proposes that different neurons discretely distributed in a certain brain region (i.e. mPOA) respond differently to stimuli (sensory and hormonal), and can eventually trigger appropriate behavioral outputs to permit the animal to express two motivations and behaviors at the same time. This review proposes several experiments to contribute to our understanding of the complex functioning of the brain. Finally, the present discussion also incorporates into these neural models the role of cortical regions in the organization of, and switching between, different behaviors or motivations.

Acknowledgments

The authors want to thank the institutions and organizations that supported the Workshop *Neural Basis of Maternal Motivation: Relationship and Coordination with other social motivational systems* and provided funds for the participation of investigators and students. We thank the School of Medicine (UdelaR) that hosted the meeting, and the Comisión Sectorial de Investigación Científica (CSIC, UdelaR), the French Embassy, the International Brain Research Organization (IBRO), and the Programme for the Development of Basic Sciences (PEDECIBA, Uruguay) for their financial support.

References

Afonso, V.M., Sison, M., Lovic, V., Fleming, A.S., 2007. Medial prefrontal cortex lesions in the female rat affect sexual and maternal behavior and their sequential organization. Behav. Neurosci. 121, 515–526.

Afonso, V.M., Grella, S.L., Chatterjee, D., Fleming, A.S., 2008. Previous maternal experience affects accumbal dopaminergic responses to pup-stimuli. Brain Res. 1198, 115–123.

Afonso, V.M., King, S., Chatterjee, D., Fleming, A.S., 2009. Hormones that increase maternal responsiveness affect accumbal dopaminergic responses to pup- and food-stimuli in the female rat. Horm. Behav. 56 (1), 11–23.

Afonso, V.M., King, S.J., Novakov, M., Burton, C.L., Fleming, A.S., 2011. Accumbal dopamine function in postpartum rats that were raised without their mothers. Horm. Behav. 60 (5), 632–643.

Afonso, V.M., Shams, W., Jin, D., Fleming, A.S., 2013. Distal pup cues evoke DA responses in hormonally-primed rats in the absence of pup-experience or ongoing maternal behavior. J. Neurosci. 33 (6), 2305–2312.

Agmo, A., 1999. Sexual motivation-an inquiry into events determining the occurrence of sexual behavior. Behav. Brain Res. 105 (1), 129–150.

Agrati, D., Fernandez-Guasti, A., Ferreira, A., 2008. The reproductive stage and experience of sexually receptive mothers alter the preference for pups or males. Behav. Neurosci. 122, 998–1004.

Agrati, D., Fernández-Guasti, A., Ferreño, M., Ferreira, A., 2011. Coexpression of sexual behavior and maternal aggression: the ambivalence of sexually active mother rats toward male intruders. Behav. Neurosci. 125 (3), 446–451.

Bauer, J.H., 1983. Effects of maternal state on the responsiveness to nest odors of hooded rats. Physiol. Behav. 30, 229–232.

Bermant, G., Westbrook, W.H., 1966. Peripheral factors in the regulation of sexual contact by female rats. J. Comp. Physiol. Psychol. 61, 244–250.

Berridge, K.C., 2000. Measuring hedonic impact in animals and infants: microstructure of affective taste reactivity patterns. Neurosci. Biobehav. Rev. 24, 173–198.

Berridge, K.C., 2004. Motivation concepts in behavioral neuroscience. Physiol. Behav. 81 (2), 179–209.

Berridge, K.C., 2006. The debate over dopamine's role in reward: the case for incentive salience. Psychopharmacology (Berl) 191 (3), 391–431.

Berridge, K.C., 2009. 'Liking' and 'wanting' food rewards: brain substrates and roles in eating disorders. Physiol. Behav. 97 (5), 537–550.

Berridge, K.C., Robinson, T.E., 1998. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? Brain Res. Rev. 28, 309–369.

Berridge, K.C., Robinson, T.E., 2003. Parsing reward. Trends Neurosci. 26 (9), 507–581.

Bindra, D., 1968. Neuropsychological interpretation of the effects of drive and incentive-motivation on general activity and instrumental behavior. Psychol. Rev. 75 (1), 1–22.

Bindra, D., 1969. A unified interpretation of emotion and motivation. Ann. N. Y. Acad. Sci. 159, 1071–1083.

Blackburn, J.R., Pfaus, J.G., Phillips, A.G., 1992. Dopamine functions in appetitive and defensive behaviours. Prog. Neurobiol. 39, 247–279.

Bridges, R.S., 1996. Biochemical basis of parental behavior in the rat. Advance in the Study of Behavior, vol. 25, 215-242. In: Rosenblatt, J.S., Snowdon, C.T. (Eds.), Parental Care: Evolution, Mechanisms, and Adaptive Significance. Academic Press.

Bruce, H.M., 1961. Observations on the suckling stimulus and lactation in the rat. J. Reprod. Fertil. 2, 17–34.

Buck, R., 1999. The biological affects: a typology. Psychol. Rev. 106 (2), 301–336.

Burgdorfa, J., Panksepp, J., Moskala, J.R., 2011. Frequency-modulated 50 kHz ultrasonic vocalizations: a tool for uncovering the molecular substrates of positive affect. Neurosci. Biobehav. Rev. 35, 1831–1836.

Byrnes, E.M., Rigero, B.A., Bridges, R.S., 2002. Dopamine antagonists during parturition disrupt maternal care and the retention of maternal behavior in rats. Pharmacol. Biochem. Behav. 73 (4), 869–875.

Cacioppo, J.T., Gardner, W.L., Berntson, G.G., 1997. Beyond bipolar conceptualizations and measures: the case of attitudes and evaluative space. Pers. Soc. Psychol. Rev. 1, 3–13.

Cacioppo, J.T., Gardner, W.L., Berntson, G.G., 1999. The affect system has parallel and integrative processing components: form follows function. J. Pers. Soc. Psychol. 76, 839–855.

Champagne, F.A., Chretien, P., Stevenson, C.W., Zhang, T.Y., Gratton, A., Meaney, M.J., 2004. Variations in nucleus accumbens dopamine associated with individual differences in maternal behavior in the rat. J. Neurosci. 24 (17), 4113–4123.

Colombetti, G., 2005. Appraising valance. J. Conscious. Stud. 12 (8–10), 103–112.

Connor, J.R., Davis, H.R., 1980. Postpartum estrus in Norway rats. I. Behav. Biol. Reprod. 23, 994–999.

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

Coria-Avila, G.A., Pfaus, J.G., 2007. Neuronal activation by stimuli that predict sexual reward in female rats. Neuroscience 148, 623–632.

Cosnier, J., 1963. Several problems posed by induced maternal behavior in rats. C. R. Seances Soc. Biol. Fil. 157, 1611–1613.

Craig, W., 1918. Appetites and aversions as constituents of instincts. Biol. Bull. Woods Hole 34, 91–107.

Cramer, C.P., Thiels, E., Alberts, J.R., 1990. Weaning in rats: I. Maternal behavior. Dev. Psychobiol. 23 (6), 479–493.

Da Costa, A.P., Guevara-Guzman, R.G., Ohkura, S., Goode, J.A., Kendrick, K.M., 1996. The role of oxytocin release in the paraventricular nucleus in the control of maternal behaviour in the sheep. J. Neuroendocrinol. 8 (3), 163–177.

D'cunha, T.M., King, S.J., Fleming, A.S., Lévy, F., 2011. Oxytocin receptors in the nucleus accumbens shell are involved in the consolidation of maternal memory in postpartum rats. Horm. Behav. 59 (1), 14–21.

Erskine, M.S., Barfield, R.J., Goldman, B.D., 1978. Intraspecific fighting during late pregnancy and lactation in rats and effects of litter removal. Behav. Biol. 23, 206–213.

Everitt, B.J., Cardinal, R.N., Parkinson, J.A., Robbins, T.W., 2003. Appetitive behavior. Impact of amygdala-dependent mechanisms of emotional learning. Ann. N. Y. Acad. Sci. 985, 233–250.

Febo, M., Felix-Ortiz, A.C., Johnson, T.R., 2010. Inactivation or inhibition of neuronal activity in the medial prefrontal cortex largely reduces pup retrieval and grouping in maternal rats. Brain Res. 1325, 77–88.

Ferreira, A., Hansen, S., 1986. Sensory control of maternal aggression in *Rattus norvegicus*. J. Comp. Psychol. 2, 173–177.

Fleming, A.S., Cheung, U., Myhal, N., Kessler, Z., 1989. Effects of maternal hormones on timidity and attraction to pup-related odors in female rats. Physiol. Behav. 46, 449–453.

Fleming, A.S., Korsmit, M., Deller, M., 1994. Rat pups are potent reinforcers to the maternal animal: effect of experience, parity, hormones, and dopamine function. Psychobiology 22 (1), 44–53.

Fleming, A.S., Ruble, D., Krieger, H., Wong, P.Y., 1997. Hormonal and experiential correlates of maternal responsiveness during pregnancy and the puerperium in human mothers. Horm. Behav. 31 (2), 145–158.

Garris, P.A., Rebec, G.V., 2002. Modeling fast dopamine neurotransmission in the nucleus acumbens during behavior. Behav. Brain Res. 137, 47–63.

Gilbert, A.N., Pelchat, R., Adler, N.T., 1980. Postpartum copulatory and maternal behaviour in Norway rats under seminatural conditions. Anim. Behav. 28, 989–995.

Gilbert, A.N., Pelchat, R.J., Adler, N.T., 1984. Sexual and maternal behavior at the postpartum oestrus: the role of the experience in time-sharing. Anim. Behav. 32, 1045–1053.

Giordano, A.L., Johnson, A.E., Rosenblatt, J.S., 1990. Haloperidol-induced disruption of retrieval behavior and reversal with apomoprhine in lactating rats. Physiol. Behav. 48, 211–214.

González-Mariscal, G., 2007. Mother rabbits and their offspring: timing is everything. Dev. Psychobiol. 49, 71–76.

González-Mariscal, G., Díaz-Sánchez, V., Melo, A.I., Beyer, C., Rosenblatt, J.S., 1994. Maternal behavior in New Zealand white rabbits: quantification of somatic events, motor patterns and steroid plasma levels. Physiol. Behav. 55, 1081–1089.

González-Mariscal, G., Chirino, R., 2011. Exposure to pup odors before mating promotes attraction to such scents across pregnancy in rabbits. In: Society for Behavioral Neuroendocrinology 15th Annual Meeting, Querétaro, México, Abstract P2.23.

González-Mariscal, G., Gallegos, J.A., Sierra-Ramírez, A., Garza Flores, J., 2009. Impact of concurrent pregnancy and lactation on maternal nest-building, estradiol and progesterone concentrations in rabbits. World Rabbit Sci. 17, 145–152.

González-Mariscal, G., Melo, A.I., Jiménez, P., Beyer, C., Rosenblatt, J.S., 1996. Estradiol, progesterone, and prolactin facilitate maternal nest-building in rabbits. J. Neuroendocrinol. 8, 901–907.

González-Mariscal, G., Poindron, P., 2002. Parental care in mammals: immediate internal and sensory factors of control. In: Pfaff, D., Arnold, A., Etgen, A., Fahrbach, S., Rubin, R. (Eds.), Hormones, Brain and Behavior. Academic Press, San Diego, pp. 215–298.

González-Mariscal, G., Rosenblatt, J.S., 1996. Maternal behavior in rabbits: a historical and multidisciplinary perspective. In: Rosenblatt, J.S., Snowdon, C.T. (Eds.), Parental Care: Evolution, Mechanisms and Adaptive Significance, Vol. 25. Academic Press, San Diego, pp. 333–360.

Grace, A.A., 1995. The tonic/phasic model of dopamine system regulation:its relevance for understanding how stimulant abuse can alter basal ganglia function. Drug Alcohol Depend. 37, 111–129.

Groenewegen, H.J., Wright, C.I., Beijer, A.V.J., 1996. The nucleus accumbens: gateway for limbic structures to reach the motor system? Chapter 29. In: Holstege, G., Bandler, R., Saper, C.B. (Eds.), Progress in Brain Research, vol. 107. Elsevier Science.

Grosvenor, C., Mena, F., 1974. Neural and hormonal control of milk secretion and milk ejection. In: Larson, B.L., Smith, V.R. (Eds.), Lactation: A Comprehensive Treatise. Academic Press, New York, pp. 227–276.

Hansen, S., Harthon, C., Wallin, E., Lofberg, L., Svensson, K., 1991a. The effects of 6-OHDA-induced dopamine depletions in the ventral or dorsal striatum on maternal and sexual behavior in the female rat. Pharmacol. Biochem. Behav. 39, 71–77.

Hansen, S., Harthon, C., Wallin, E., Lofberg, L., Svensson, K., 1991b. Mesotelencephalic dopamine system and reproductive behavior in the female rat: effects of ventral tegmental 6-hydroxydopamine lesions on maternal and sexual responsiveness. Behav. Neurosci. 105 (4), 588–598.

Hansen, S., Bergvall, A.H., Nyiredi, S., 1993. Interaction with pups enhances dopamine release in the ventral striatum of maternal rats: a microdialysis study. Pharmacol. Biochem. Behav. 45, 673–676.

Harmon, K.M., Cromwell, H.C., Burgdorf, J., Moskal, J.R., Brudzynski, S.M., Kroes, R.A., Panksepp, J., 2008. Rats selectively bred for low levels of 50 kHz ultrasonic vocalizations exhibit alterations in early social motivation. Dev. Psychobiol. 50, 322–331.

Hauser, H., Gandelman, R., 1985. Lever pressing for pups: evidence for hormonal influence upon maternal behavior of mice. Horm. Behav. 19, 454–468.

Ikemoto, S., Panksepp, J., 1999. The role of nucleus accumbens dopamine in motivated behavior: a unifying interpretation with special reference to reward-seeking. Brain Res. Rev. 31, 6–41.

Jakubowski, M., Terkel, J., 1985. Incidence of pup killing and parental behavior in virgin female and male rats (*Rattus norvegicus*): differences between Wistar and Sprague-Dawley stocks. J. Comp. Psychol. 99 (1), 93–97.

Jilge, B., 1993. The ontogeny of circadian rhythms in the rabbit. J. Biol. Rhythms 8, 247–260.

Jilge, B., 1995. Ontogeny of the rabbit's circadian rhythms without an external zeitgeber. Physiol. Behav. 58, 131–140.

Joseph, M.H., Datla, K., Young, A.M., 2003. The interpretation of the measurement of nucleus accumbens dopamine by in vivo dialysis: the kick, the craving or the cognition? Neurosci. Biobehav. Rev. 27 (6), 527–541.

Kalivas, P.W., Volkow, N.D., 2005. The neural basis of addiction: a pathology of motivation and choice. Am. J. Psychiatry 162, 1403–1413.

Keer, S.E., Stern, J.M., 1999. Dopamine receptor blockade in the nucleus accumbens inhibits maternal retrieval and licking, but enhances nursing behavior in lactating rats. Physiol. Behav. 67 (5), 659–669.

Kelly, A.E., 2004. Memory and addiction: Sahred neural circuitry and molecular mechanisms. Neuron 44, 161–179.

Kendrick, K.M., Keverne, E.B., Baldwin, B.A., 1987. Intracerebroventricular oxytocin stimulates maternal behaviour in the sheep. Neuroendocrinology 46 (1), 56–61.

Kendrick, K.M., Keverne, E.B., Hinton, M.R., Goode, J.A., 1992. Oxytocin, aminoacid and monoamine release in the region of the medial preoptic area and bed nucleus of the stria terminalis of the sheep during parturition and suckling. Brain Res. 569, 199–209.

Keverne, E.B., 1996. The psychopharmacology of maternal behaviour. J. Psychopharmacol. 10, 16–22.

Kinsley, C.H., Bridges, R.S., 1990. Morphine treatment and reproductive condition alter olfactory preferences for pup and adult male odors in female rats. Dev. Psychobiol. 23 (4), 331–347.

Kristal, M.B., 1980. Placentophagia: a biobehavioral enigma (or De gustibus non diputandum est). Neurosci. Biobehav. Rev. 15, 425–435.

Kuroda, K.O., Tachikawa, K., Yoshida, S., Tsuneoka, Y., Numan, M., 2011. Neuromolecular basis of parental behavior in laboratory mice and rats: With special emphasis on technical issues of using mouse genetics. Prog. Neuropsychopharmacol. Biol. Psychiatry 35 (5), 1205–1231.

Lee, A., Clancy, S., Fleming, A.S., 1999. Mother rats bar-press for pups: effects of lesions of the mpoa and limbic sites on maternal behavior and operant responding for pup-reinforcement. Behav. Brain Res. 10, 15–31.

Lévy, F., Poindron, P., Le Neindre, P., 1983. Attraction and repulsion by amniotic fluids and their olfactory control in the ewe around parturition. Physiol. Behav. 31 (5), 687–692.

Lévy, F., Kendrick, K.M., Keverne, E.B., Piketty, V., Poindron, P., 1992. Intracerebral oxytocin is important for the onset of maternal behavior in inexperienced ewes delivered under peridural anesthesia. Behav. Neurosci. 106 (2), 427–432.

Lin, D., Boyle, M.P., Dollar, P., Lee, H., Lein, E.S., Perona, P., Anderson, D.J., 2011. Functional identification of an aggression locus in the mouse hypothalamus. Nature 470, 221–227.

Lonstein, J.S., 2002. Effects of dopamine receptor antagonism with haloperidol on nurturing behavior in the biparental prairie vole. Pharmacol. Biochem. Behav. 74, 11–19.

Louilot, A., Le Moal, M., Simon, H., 1986. Differential reactivity of dopaminergic neurons in the nucleus accumbens in response to different behavioral situations, an in vivo voltammetric study in free moving rats. Brain Res. 397, 395–400.

Lucas, B.K., Ormandy, C.J., Binart, N., Bridges, R.S., Kelly, P.A., 1998. Null mutation of the prolactin receptor gene produces a defect in maternal behavior. Endocrinology 139 (10), 4102–4107.

Machin, A.J., Dunbar, R.I.M., 2011. The brain opioid theory of social attachment: a review of the evidence. Behaviour 148, 985–1025.

Mattson, B.J., Williams, S., Rosenblatt, J.S., Morrell, J.I., 2001. Comparison of two positive reinforcing stimuli: pups and cocaine throughout the postpartum period. Behav. Neurosci. 115 (3), 683–694.

Mattson, B.J., Morrell, J.I., 2005. Preference for cocaine- versus pup-associated cues differentially activates neurons expressing either Fos or cocaine- and amphetamine-regulated transcript in lactating, maternal rodents. Neuroscience 135, 315–328.

Melo, A.I., González-Mariscal, G., 2003. Placentophagia in rabbits: incidence across the reproductive cycle. Dev. Psychobiol. 43, 37–43.

Neckers, L.M., Zarrow, M.X., Myers, M.M., Denenberg, V.H., 1975. Influence of olfactory bulbectomy and the serotonergic system upon intermale aggression and maternal behavior in the mouse. Pharmacol. Biochem. Behav. 3, 545–550.

Nelson, E.E., Panksepp, J., 1998. Brain substrates of infant-mother attachment: contributions of opioids, oxytocin, and norepinephrine. Neurosci. Biobehav. Rev. 22 (3), 437–452.

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003

Newman, S.W., 1999. The medial extended amygdala in male reproductive behavior. A node in the mammalian social behavior network. Ann. N. Y. Acad. Sci. 877, 242–257.

Norris, C.J., Gollan, J., Berntson, G.G., Cacioppo, J.T., 2010. The current status of research on the structure of evaluative space. Biol. Psychol. 84, 422–436.

Nowak, R., Keller, S.M., Lévy, F., 2011. Mother–young relationships in sheep: a model for a multidisciplinary approach of the study of attachment in mammals. J. Neuroendocrinol. 23, 1042–1053.

Numan, M., 2006. Hypothalamic neural circuits regulating maternal responsiveness toward infants. Behav. Cogn. Neurosci. Rev. 5, 163–190.

Numan, M., Insel, T.R., 2003. The Neurobiology of Parental Behavior. Springer-Verlag, New York, Inc.

Numan, M., Numan, M.J., Pliakou, N., Stolzenberg, D.S., Mullins, O.J., Murphy, J.M., Smith, C.D., 2005a. The effects of D1 or D2 dopamine receptor antagonism in the medial preoptic area, ventral pallidum, or nucleus accumbens on the maternal retrieval response and other aspects of maternal behavior in rats. Behav. Neurosci. 119 (6), 1588–1604.

Numan, M., Numan, M.J., Schwarz, J.M., Neuner, C.M., Flood, T.F., Smith, C.D., 2005b. Medial preoptic area interactions with the nucleus accumbens-ventral pallidum circuit and maternal behavior in rats. Behav. Brain Res. 158 (1), 53–68.

Numan, M., Fleming, A.S., Lévy, F., 2006. Maternal behavior. In: Neill, J.D. (Ed.), Knobil and Neill's Physiology of Reproduction. Elsevier, San Diego, pp. 1921–1993.

Numan, M., Stolzenberg, D.S., 2009. Medial preoptic area interactions with dopamine neural systems in the control of the onset and maintenance of maternal behavior in rats. Front. Neuroendocrinol. 30, 46–64.

Numan, M., Woodside, B., 2010. Maternity: neural mechanisms, motivational processes, and physiological adaptations. Behav. Neurosci. 124 (6), 715–741.

Olazábal, D.E., 2010. Stability and potential inheritance of infanticidal behavior in prairie voles. Dev. Psychobiol. 52 (8), 825–832.

Olazábal, D.E., Pereira, M., Agrati, D., Ferreira, A., Fleming, A.S., González-Mariscal, G., Lévy, F., Lucion, A.B., Morrell, J.I., Numan, M., Uriarte, N., 2013. Flexibility and adaptation of the neural substrate that supports maternal behavior in mammals. Neurosci. Biobehav. Rev., http://dx.doi.org/10.1016/j.neubiorev.2013.04.004, in press.

Olazábal, D.E., Young, L.J., 2005. Variability in spontaneous maternal behavior is associated with anxiety-like behavior and affiliation in naïve juveniles and adult female prairie voles (*Microtus ochrogaster*). Dev. Psychobiol. 47, 166–178.

Parada, M., King, S., Li, M., Fleming, A.S., 2008. The roles of accumbal dopamine D1 and D2 receptors in maternal memory in rats. Behav. Neurosci. 122 (2), 368–376.

Paredes, R.G., Alonso, A., 1997. Sexual behavior regulated (paced) by the female induces conditioned place preference. Behav. Neurosci. 111, 123–128.

Parker, J.G., Zweifel, L.S., Clark, J.J., Evans, S.B., Phillips, P.E., Palmiter, R.D., 2010. Absence of NMDA receptors in dopamine neurons attenuates dopamine release but not conditioned approach during Pavlovian conditioning. Proc. Natl. Acad. Sci. U.S.A. 107 (30), 13491–13496.

Pedersen, C.A., Prange Jr., A.J., 1979. Induction of maternal behavior in virgin rats after intracerebroventricular administration of oxytocin. Proc. Natl. Acad. Sci. U.S.A. 76 (12), 6661–6665.

Pennartz, C.M.A., Groenewegen, H.J., Lopes Da Silva, F.H., 1994. The nucleus accumbens as a complex of functionally distinct neuronal ensembles: an integration of behavioral, electrophysiological and anatomical data. Prog. Neurobiol. 42, 719–761.

Pereira, M., Ferreira, A., 2006. Demanding pups improve maternal behavioral impairments in sensitized and haloperidol-treated lactating female rats. Brain Res. 175, 139–148.

Pereira, M., Morrell, J.I., 2011. Functional mapping of the neural circuitry of rat maternal motivation: effects of site-specific transient neural inactivation. J. Neuroendocrinol. 23 (11), 1020–1035.

Pereira, M., Farrar, A.M., Abercrombie, E.D., Morrell, J.I., 2011. Role of nucleus accumbens core dopamine in rat maternal responsiveness. In: Society for Neuroscience, 41th Annual Meeting, Washington DC.

Pfaff, D.W., 1982. Motivational concepts: definitions and distinctions. In: Pfaff, D.W. (Ed.), The Physiological Mechanisms of Motivation. Springer-Verlag, New York, pp. 3–24.

Poindron, P., Le Neindre, P., 1980. Endocrine and sensory regulation of maternal behavior in the ewe. Adv. Study Behav. 11, 75–119.

Pryce Ch, R., Dobeli, M., Martin, R.D., 1993. Effects of sex steroids on maternal motivation in the common marmoset (*Callithrix jacchus*): development and application of an operant system with maternal reinforcement. J. Comp. Psychol. 107, 99–115.

Redgrave, P., Prescott, T.J., Gurney, K., 1999. Is the short-latency dopamine response too short to signal reward error? TINS 22 (4), 146–151.

Reisbick, S., Rosenblatt, J.S., Mayer, A.D., 1975. Decline of maternal behavior in the virgin and lactating rat. J. Comp. Physiol. Psychol. 89, 722–732.

Reynolds, S.M., Berridge, K.C., 2008. Emotional environments retune the valence of appetitive versus fearful functions in nucleus accumbens. Nat. Neurosci. 11, 423–425.

Robbins, T.W., Everitt, B.J., 1996. Neurobehavioural mechanisms of reward and motivation. Curr. Opin. Neurobiol. 6, 228–236.

Robinson, D.L., Zitzman, D.L., Williams, S.K., 2011. Mesolimbic dopamine transients in motivated behaviors: focus on maternal behavior. Front. Psychiatry 2, 23.

Rosenblatt, J.S., 1967. Non-hormonal basis of maternal behavior in the rat. Science 156, 1512–1514.

Rosenblatt, J.S., Siegel, H., 1981. Factors governing the onset and maintenance of maternal behavior among non-primate mammals. In: Gubernick, D.J., Klopfer, P.H. (Eds.), Parental Care in Mammals. Plenum Press, New York, pp. 13–76.

Rougé-Maillart, C., Jousset, N., Gaudin, A., Bouju, B., Penneau, M., 2005. Women who kill their children. Am. J. Forensic. Med. Pathol. 26 (4), 320–326.

Salamone, J.D., Correa, M., 2002. Motivational views of reinforcement: implications for understanding the behavioral functions of nucleus accumbens dopamine. Behav. Brain Res. 137, 3–25.

Saltzman, W., Maestripieri, D., 2011. The neuroendocrinology of primate maternal behavior. Prog. Neuropsychopharmacol. Biol. Psychiatry 35 (5), 1192–1204.

Schultz, W., Dayan, P., Montague, P.R., 1997. A neural substrate of prediction and reward. Science 275, 1593–1599.

Sesack, S.R., Grace, A.A., 2010. Cortico-basal ganglia reward network: microcircuitry. Neuropsychopharmacology 35 (1), 27–47.

Smith, K.S., Berridge, K.C., Aldridge, J.W., 2011. Disentangling pleasure from incentive salience and learning signals in brain reward circuitry. Proc. Natl. Acad. Sci. U.S.A. 108 (27), E255–E264.

Stack, E.C., Balakrishnan, R., Numan, M.J., Numan, M., 2002. A functional neuroanatomical investigation of the role of the medial preoptc area in the neural circuits regulating maternal behavior. Behav. Brain Res. 131, 17–36.

Steiner, J., Glaser, D., Hawilo, M.H., Berridge, K.C., 2001. Comparative expression of hedonic impact: affective reactions to taste by human infants and other primates. Neurosci. Biobehav. Rev. 25, 53–74.

Stern, J.M., 1996. Somatosensation and maternal care in Norway rats. In: Rosenblatt, J.S., Snowdon, C.T. (Eds.), Advances in the Study of Behavior, 25. Academic Press, San Diego, pp. 243–294.

Stern, J.M., Keer, S.E., 1999. Maternal motivation of lactating rats is disrupted by low dosages of haloperidol. Behav. Brain Res. 99, 231–239.

Stern, J.M., Taylor, L.A., 1991. Haloperidol inhibits maternal retrieval and licking, but enhances nursing behavior and litter weight gains in lactating rats. J. Neuroendocrinol. 3 (6), 591–596.

Stolzenberg, D.S., McKenna, J.B., Keough, S., Hancock, R., Numan, M.J., Numan, M., 2007. Dopamine D1 receptor stimulation of the nucleus accumbens or the medial preoptic area promotes the onset of maternal behavior in pregnancy-terminated rats. Behav. Neurosci. 121 (5), 907–919.

Stolzenberg, D.S., Numan, M., 2011. Hypothalamic interaction with the mesolimbic DA system in the control of the maternal and sexual behaviors in rats. Neurosci. Biobehav. Rev. 35, 826–847.

Teitelbaum, P., 1966. The use of operant methods in the assessment and control of motivational states. In: Honig, W.K. (Ed.), Operant Behavior: Areas of Research and Application. Appleton-Century-Crofts, New York, pp. 565–608.

Teitelbaum, P., 1977. Levels of integration of the operant. In: Honig, W.K., Staddon, J.E.R. (Eds.), Handbook of Operant Behavior. Prentice-Hall, Englewood Cliffs (NJ), pp. 7–27.

Terkel, J., Bridges, R.S., Sawyer, C.H., 1979. Effects of transecting lateral neural connections of the medial preoptic area on maternal behavior in the rat: nest building, pup retrieval and prolactin secretion. Brain Res. 169 (2), 369–380.

Uvnäs-Moberg, K., 1998. Oxytocin may mediate the benefits of positive social interaction and emotions. Psychoneuroendocrinology 23 (8), 819–835.

Vandenbergh, J.C., 1973. Effects of central and peripheral anosmia on reproduction of female mice. Physiol. Behav. 10, 257–261.

Veening, J.G., Coolen, L.M., de Jong, T.R., Joosten, H.W., de Boer, S.F., Koolhaas, J.M., Olivier, B., 2005. Do similar neural systems subserve aggressive and sexual behaviour in male rats? Insights from c-Fos and pharmacological studies. Eur. J. Pharmacol. 526 (1–3), 226–239.

Wansaw, M.P., Pereira, M., Morrell, J.I., 2008. Characterization of maternal motivation in the lactating rat: contrasts between early and late postpartum responses. Horm. Behav. 54 (2), 294–301.

Wilsoncroft, W.E., 1969. Babies by bar-press: maternal behavior in the rat. Behav. Res. Meth. Instrument. 1, 229–230.

Wise, R.A., 2008. Dopamine and reward: the anhedonia hypothesis 30 years on. Neurotox. Res. 14 (2–3), 169–183.

Wolff, M.E., 2002. Addiction: making the connection between behavioral changes and neuronal plasticity in specific pathways. Mol. Interv. 3 (2), 146–157.

Yizhar, O., Fenno, L.E., Davidson, T.J., Mogri, M., Deisseroth, K., 2011. Optogenetics in neural systems. Neuron 71, 9–34.

Zhao, C., Li, M., 2010. c-Fos identification of neuroanatomical sites associated with haloperidol and clozapine disruption of maternal behavior in the rat. Neuroscience 166 (4), 1043–1055.

Please cite this article in press as: Olazábal, D.E., et al., New theoretical and experimental approaches on maternal motivation in mammals. Neurosci. Biobehav. Rev. (2013), http://dx.doi.org/10.1016/j.neubiorev.2013.04.003