Hormones and Behavior 77 (2016) 30–41

Contents lists available at ScienceDirect

Hormones and Behavior

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

Review article

Mothers and offspring: The rabbit as a model system in the study of mammalian maternal behavior and sibling interactions

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ARTICLE INFO

Available online 7 June 2015

Keywords:
Suckling
Siblings
Circadian
Pregnancy
Light–dark cycle
Nest-building
Estradiol
Progesterone
Prolactin
Oxytocin

ABSTRACT

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

Jay Rosenblatt effectively promoted research on rabbit maternal behavior through his interaction with colleagues in Mexico. Here we review the activities of pregnant and lactating rabbits (*Oryctolagus cuniculus*), their neurohormonal regulation, and the synchronization of behavior between mother and kits. Changing concentrations of estradiol, progesterone, and prolactin throughout gestation regulate nest-building (digging, straw-carrying, fur-pulling) and prime the mother's brain to respond to the newborn. Nursing is the only mother–young contact throughout lactation. It happens once/day, inside the nest, with ca. 24 h periodicity, and lasts around 3 min. Periodicity and duration of nursing depend on a threshold of suckling as procedures reducing the amount of nipple stimulation interfere with the temporal aspects of nursing, though not with the doe's maternal motivation. Synchronization between mother and kits, critical for nursing, relies on: a) the production of pheromonal cues which guide the young to the mother's nipples for suckling; b) an endogenous circadian rhythm of anticipatory activity in the young, present since birth. Milk intake entrains the kits' locomotor behavior, corticosterone secretion, and the activity of several brain structures. Sibling interactions within the huddle, largely determined by body mass at birth, are important for: a) maintaining body temperature; b) ensuring normal neuromotor and social development. Suckling maintains nursing behavior past the period of abundant milk production but abrupt and efficient weaning occurs in concurrently pregnant-lactating does by unknown factors. Conclusion: female rabbits have evolved a reproductive strategy largely dissociating maternal care from maternal presence, whose multifactorial regulation warrants future investigations.

Contents

Abbreviations: CORT, corticosterone; EB, estradiol benzoate; ER, estradiol receptor alpha; FAA, food-anticipatory activity; icv, intracerebroventricular; IR, immunoreactive; MB, maternal behavior; OT, oxytocin; OVX, ovariectomized; POA, preoptic area; PR, progesterone receptor; PRL, prolactin; PVN, paraventricular nucleus; SCN, suprachiasmatic nucleus; T, testosterone; THELX, thelectomy.

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http://dx.doi.org/10.1016/j.yhbeh.2015.05.011
0018-506X/

Introduction

Jay Rosenblatt had a decisive influence on the development of research on the reproductive behavior of the European rabbit (*Oryctolagus cuniculus*) in Tlaxcala and Veracruz (Mexico), where the five co-authors of this manuscript have worked for many years. Jay had shown that, in laboratory rats (*Rattus norvegicus*), mother–young contact at parturition and across early lactation (rather than any specific hormone) was crucial for the consolidation of maternal behavior (MB; Rosenblatt and Siegel, 1981). However, because rats interact intensely with the litter for several hours/day, he wanted to test the validity of his hypothesis in species showing shorter episodes of maternal care. As early work (Deutsch, 1957; Lincoln, 1974; Zarrow et al., 1965) had shown that doe rabbits nurse their young for only a few minutes/day Jay thought they would be an ideal model for his study purpose. Jay knew the Mexican endocrinologist Carlos Beyer and the early work he had done on the neuroendocrinology of domestic rabbit lactation (Mena and Beyer, 1963; Tindal et al., 1963). In his new location in Tlaxcala, Carlos had a large colony of rabbits and when Jay visited it (in 1989), they agreed to launch a line of research on behavioral neuroendocrinology in mother rabbits.

In another corner of the world Jay met Robyn Hudson, who was doing research in Munich (with Hans Distel) on the circadian behavior of rabbit kits and their dependence on an olfactory signal from the mother's belly to find the nipples and suckle (Hudson and Distel, 1982, 1983, 1984, 1986, 1989, 1990; Distel and Hudson, 1985). Jay persuaded Robyn to come to Tlaxcala and be part of an international rabbit research team that was gradually taking form. Thus, under Jay's and Carlos' influence we planned and performed the first experiments in Tlaxcala on neuroendocrine regulation of rabbit MB (González-Mariscal et al., 1994b, 1996). In this new venue Robyn met Margarita Martínez-Gómez, who had recently graduated from our Masters in Science program and was starting a new research center at the Autonomous University of Tlaxcala. The two of them initiated another line of investigation, focusing on the newborn kits with the incorporation of Amando Bautista. Later on their research extended beyond laboratory animals, exploring the behavior of wild rabbits both in Europe (*O. cuniculus*;) and in Tlaxcala (*Silvilagus floridanus and S. cunicularius*), including at the field station established at the volcano of *La Malinche* (Aguilar et al., 2014; Hudson et al., 2005; Rodríguez-Martínez et al., 2014; Vázquez et al., 2007).

Another graduate from our program, Mario Caba, went to Rae Silver's laboratory at Columbia University to train in chronobiology and immunocytochemistry. Back at the University of Veracruz he has developed his own line of research exploring the variety of signals that allow the synchronization of the behavior of mother and kits.

The European rabbit is important in animal production (González-Mariscal et al., 2007), as a pet, and as an agricultural pest. It is also a classical species in biomedical and psychobiological research (Ramírez and Beyer, 1988) and it is one of the best studied of all laboratory mammals in the wild (González-Redondo et al., in press; Harcourt-Brown, 2002; Manning et al., 1994; McNitt et al., 2000; Thompson and King, 1994). In particular, due to its proverbial reproductive powers and tightly organized pattern of female reproductive physiology and behavior, the rabbit provides a particularly good opportunity to study the neuroendocrine mechanisms regulating mammalian maternal care and their underlying temporal coordination. Much of this information is widely scattered across journals representing very different disciplines, and remembering Jay Rosenblatt provides a timely opportunity to review this literature to which he contributed so importantly.

Nest-building

Gestation in the rabbit lasts 30 to 32 days and the litters range in size from typically 3 to 6 altricial kits in the wild (Eccard and Rödel, 2011; Rödel et al., 2008a,2008c; Thompson and King, 1994), and 4 to 10 or more in domestic breeds (Manning et al., 1994; McNitt et al., 2000; Schlolaut et al., 2013). Maternal behavior begins with the mother digging a nursery burrow or a chamber in the communal warren on about day 25 or 26 of gestation (Deutsch, 1957; Lloyd and McCowan,

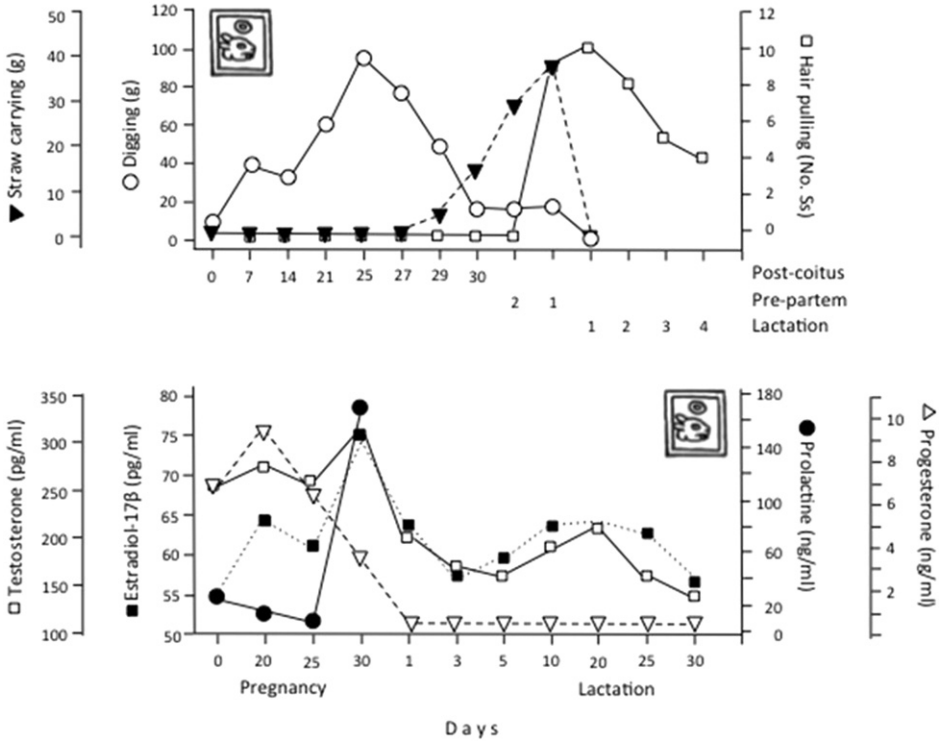

Fig. 1. Temporal coincidence between variations in specific nest-building activities and concentrations of particular hormones in the blood of pregnant and lactating rabbits. Prolactin concentrations taken from McNeilly and Friessen (1978). Modified from González-Mariscal et al. (1994b). Insert: glyph from the Mexica tribes' calendar indicating the year rabbit 1; introduced to honor Prof. J.S. Rosenblatt in the first publication on rabbit maternal behavior we produced together.