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Maternal alterations induced by exposure to an unfamiliar home cage in early underfed dams

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ABSTRACT

The expression of different behavioral components in the adult rat depends on a number of early influences, including age, hormones, manipulations of sensory cues, and perinatal undernutrition, all of which impact the development of brain areas underlying adaptive processes, maternal behavior, and the response to novelty. The current study investigates the effects of pre- and neonatal undernutrition on various components of maternal behavior of dams exposed to the challenge of an unfamiliar home cage on days 4, 8, and 12 of lactation. Food restriction was initiated from gestational day (G) G6 to G19 when dams received 50–70% of the normal balanced diet, followed by 100% from G20 to G21. After birth, pups were underfed by alternating every 12 h between two lactating dams, one of which, had ligated nipples. Weaning was at 25 days of age followed by an *ad libitum* diet until postpartum day 90, when females were mated, and subsequently tested for maternal behavior in an unfamiliar cage. The results indicated that in early underfed mothers the frequency of handling wood shavings and of, approaching, licking, crouching, and grasping pups for retrieval was significantly reduced. Moreover, self-grooming increased substantially in the underfed dams, but the frequency of rearing was reduced. Additionally, the body weight of pups nursed by early underfed dams was significantly lower than that of control pups. These findings suggest a relation between early food restriction and the deficient maternal care observed when these dams were challenged by exposure to an unfamiliar home cage.

1. Introduction

Maternal behavior in rodents is a complex repertoire of responses that promote the survival of the offspring by providing them with adequate warmth and a comfortable nest, frequent body licking, retrieval, breast feeding, and protection under a crouching mother (Fleming et al., 1999; Douglas, 2010). When mother leaves the litter, or is separated from the pups, they frequently emit ultrasonic calls at 30–50 kHz, and the dam retrieves them to the nest, calming and reducing the distress response (Oswalt and Meier, 1975; Okabe et al., 2013; Yoshida et al., 2013). Thus, early lactation is a fundamental stage of the dam's lifespan; through an intense mother-litter interaction, the dam sustains the litter by nursing, promoting its physical development, and exposing it to early learning experiences that influence their brain growth and function, as well as the affective responses that may be expressed as adaptive responses in later stages of life (Moriceau and Sullivan, 2006; Richards et al., 2012).

Several studies have shown that perinatal undernutrition (PNU) has long-lasting effects on shaping the individual's pattern of the lactating dam responses to novel, hormonal, sensory, and stress conditions including the maternal care of the young. Previous evidence indicates that the behavioral alterations produced by PNU, both in humans and in animal models, result in impaired mother-infant interactions with reduced pup´śvocal communications, reduced suckling movements, and poor sensory signals given by the underfed young, all of which elicit deficient or inadequate maternal behavioral components and disrupt hormonal and brain changes required for the dam to adapt to the challenge of an unfamiliar cage (UC) (Smart, 1976; Morgan et al., 1992; Torrero et al., 2000; Tonkiss et al., 2003; Wu et al., 2004; Lopez-Jimenez et al., 2013). Unfortunately, little information is available about the long-lasting effects of PNU and its associated negative influence on the early family environment, which is full of risk factors that may promote several mental disorders later in life (Lumey, 1998; Godfrey and Barker, 2000; Caldji et al., 2000; Levine, 2001; Kehoe et al., 2001). Nonetheless, PNU studies have focused on the alterations of different maternal behavioral components under a home cage condition. For example, the influence of sensory deprivation, body massage, or the exposure to a sensory enriched environment in PNU females

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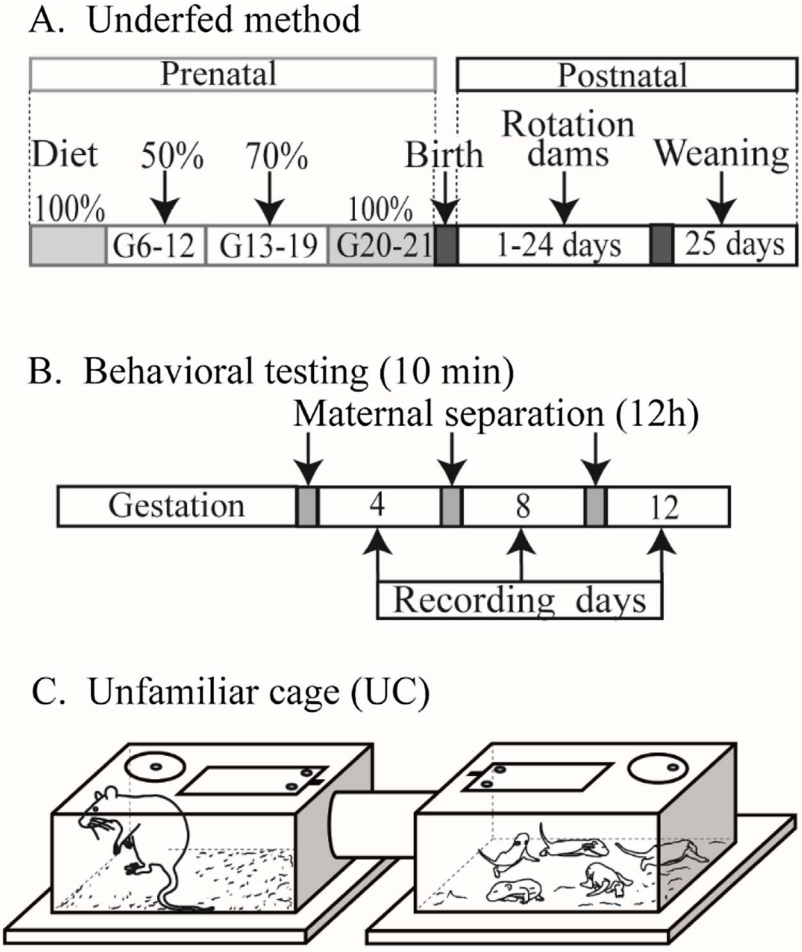

Fig. 1. Schematic representation of A, the underfed method; B, the behavioral testing and recording (10 min); C, the UC.

tested for maternal behavior in adulthood (Franková, 1973; Galler and Propert, 1981; Crnic et al., 1981; Regalado et al., 1999; Lopez-Jimenez et al., 2013; Felix et al., 2014). And although there is still little information on the effects of unfamiliar environmental conditions on maternal responses (Hess et al., 2002; D'Ámato et al., 2005), the model of lactation in underfeed dams exposed to an unfamiliar condition may be helpful to understand adaptive disruptions in this critical stage of life. The hypothesis of this study was to analyze the long-lasting effects of PNU on the maternal and non-maternal behavioral responses to the litter when the lactating dams were separated from the pups for 12 h on postnatal days 4, 8, and 12 and then exposed to the challenge of a UC, where they were reunited. We predicted that PNU dams after being separated from their pups and challenged by a UC, would decrease the expression of maternal behavioral components and increase, non-maternal responses. To our knowledge there is no information on literature about the maternal responsiveness of early underfed dams to the progeny in a UC context.

2. Methods

2.1. Animals and experimental design

Female Wistar rats (*Rattus norvegicus*), descendants of a stock originally purchased from Harlan Sprague-Dawley and subsequently bred in our laboratory at the Institute of Neurobiology, National Autonomous University of Mexico (UNAM) were used. Litters (n = 8 pups, 4 males and 4 females) were maintained under a 12-h/12-h light/dark cycle (lights on at 0800 h) in a room at 23 ± 2 °C with about 50% humidity and were housed with mothers, who had free access to standard food (Purina chow) and water. All experiments were carried out in accordance with the ethical standards defined by the local committee on animal care (Norma Oficial Mexicana NOM-062-ZOO-1999), which complies with the guidelines in the Institutional Animal Care and Use Committee Guidebook and the protocol was approved by the local Committee on Research Ethics. The number and suffering of animals was kept to a minimum. All experiments were recorded between 0900 and 1200 h (*i.e.*, during the first 4 h of the light phase of the cycle) to reduce the possible effects of circadian variations on maternal behavior.

2.2. Experimental groups

2.2.1. Control group (CG)

Twenty-four hours after the day of birth, referred to as PD 0, pups were randomly mixed, redistributed, and adjusted to 8 pups per mother (four males and four females), and the maternal responses were evaluated. The CG was made up of 16 females obtained from at least five well-nourished litters, and they were nursed by well-fed dams that had free access to water and a balanced diet (Purina chow) during gestation. After birth, CG pups were fed by two, normally lactating mothers, who were rotated every 12 h between litters until postnatal day (PD) 24. The pups were maintained in the same housing conditions until PD 90. For mating, a normal male was placed in a plastic translucent cage ($60 \times 32 \times 20$ cm^3) containing three females (200–250 g). Pregnant females were placed in individual plastic translucent maternity cages ($35 \times 27 \times 17$ cm^3) with grill tops. Wood shavings on the floor served as nesting material.

2.2.2. Undernourished group (UG)

Pups in this group were randomly mixed, redistributed, and adjusted to 8 pups per mother (four males and four females) 24 h after PD