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Physiology & Behavior 90 (2007) 353–361

PHYSIOLOGY & BEHAVIOR

# Food deprivation and the role of estradiol in mediating sexual behaviors in meadow voles

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Received 27 December 2005; received in revised form 11 September 2006; accepted 22 September 2006

**Abstract**

Female mammals are particularly sensitive to changes in food availability. The mechanisms that affect sexual behavior and food intake are closely related to one another; chief among the mechanisms that control sexual behaviors in females is estradiol. In order to understand how food deprivation results in inhibition of sexual behavior (attractivity, proceptivity, and receptivity), we measured the effects of food deprivation on circulating concentrations of estradiol. We also determined whether estradiol treatment was sufficient to restore sexual behaviors in food-deprived female meadow voles. We found that estradiol titers of food-deprived female voles are significantly lower than those of *ad lib*-fed female voles. Further, we found that estradiol treatment was sufficient to restore proceptivity and receptivity in food-deprived, ovariectomized female voles. However, estradiol treatment was not able to overcome the food deprivation-induced inhibition of attractivity. Thus, decreases in estradiol titer of food-deprived female voles may be related to the suppression of their proceptive and receptive behaviors, and may be a mechanism that allows females to avoid mating when conditions are not propitious for their survival and that of their offspring.


*Keywords:* Estradiol; Food deprivation; Sexual behavior; Odor preferences; Vole; Microtus

## 1. Introduction

Reproduction involves a significant energetic investment, especially for female mammals. As a result, female mammals inhibit sexual behavior and change physiological parameters relating to sexual behaviors when a sufficient energy supply, in the form of foodstuff, is not present in suitable quantity or quality [1–3]. The physiological mechanisms that directly or indirectly cause changes in sexual behaviors are of interest, as the mechanisms that control sexual behavior are closely associated with the frequency and amount of food intake [4].

The role that gonadal steroids play in mediating sex behaviors has been known for quite some time. Additionally, considerable interest [4–6] has focused on the effects of stressors, such as food deprivation play in mediating the synthesis of gonadatropins and gonadal hormones. For example, food deprivation or restriction interrupts the release of gonadatropin releasing hormone (GnRH) and subsequently, luteinizing hormone (LH) and follicle stimulating hormone (FSH) release; this, in turn, results in reduced secretion of gonadal steroid hormones [1,4,7]. In a number of mammalian species including mice, rats, hamsters, musk shrews, and non-human primates changes in circulating titers of gonadal steroids are induced by changes in food availability cause [3,8–10]. For example, both food-restricted female mice and musk shrews have lower gonadal steroid titers than those that are *ad lib*-fed [1,8,11]. Food-deprived intact golden hamsters have lower concentrations of circulating estradiol than do their *ad lib*-fed counterparts [4,12]. These studies, however, did not report the titers of estradiol in steroid-primed animals.

The role of estradiol in mediating sexual behavior in food-deprived and restricted females is not clear. Some studies have found that estradiol treatment reinstates short latency lordosis in food-restricted female golden hamsters [12,13]. A more recent study, however, reported that priming females with physiological amounts of estradiol was not sufficient to restore the amount of lordosis in food-deprived ovariectomized (OVX) golden hamsters, compared to those that were *ad lib*-fed [14]. Our lack of understanding in the association among food deprivation, circulating estradiol titers, and the sexual behavior of females are made even murkier by the fact that many studies

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doi:10.1016/j.physbeh.2006.09.034

on food deprivation in female mammals focus on changes in a single component of sexual behavior, usually sexual receptivity or lordosis. However, sexual behavior is more complex than receptivity alone and measurement of lordosis does not reveal if a female is or is not showing an amount of lordosis sufficient for intromission and ejaculation. For example, females must first be attractive to males and display behaviors that elicit proceptive behaviors from males [15]. In rodents, attractivity is associated with the production and secretion of odors by females that are attractive to males and proceptivity is associated with the male's response or odor preferences for particular females [3,15–22]. We have shown that after acute food deprivation female voles were no longer attractive to males, did not display proceptive behaviors when they encounter scent marks of males, and did not copulate with male voles [22,23].

Currently, we know little about the effects of acute food deprivation on more than a single component of sexual behavior in other mammals. Further, we do not know whether suppression of sexual behavior of food-deprived female voles is associated with a reduction in their circulating titers of estradiol. Estradiol has been found to be necessary and sufficient for the display of sexual behaviors in female meadow voles [16,24], similar to that for females in other species [1]. However, the amount of time required for female meadow voles to inhibit and subsequently recover sexual behaviors with re-feeding, were not the same were found with other species [22,23]. Such differences may be attributed to species differences in the endocrine and reproductive physiology that mediate sexual behavior of these small mammals. Nevertheless, the available data suggest that changes in circulating titer of estradiol may be a mechanism that underlies changes in sexual behavior in food-deprived or restricted female mammals [3,10,11]. The goal of the present study was to address the following two questions. 1) Is acute food deprivation sufficient to lower circulating titers of estradiol of female voles? 2) Is exogenous estradiol sufficient for female meadow voles to overcome the inhibitory effects of food deprivation on the three components of sexual behavior? To address these questions we tested the hypothesis that the expression of sexual behavior of food-deprived female voles is associated with their circulating titers of estradiol. This hypothesis makes the following predictions. 1) Acute food deprivation is sufficient to induce female meadow voles to have lower circulating titers of estradiol relative to female voles that were not food-deprived. 2) Exogenous estradiol is sufficient for female meadow voles to overcome the inhibitory effects of food deprivation on the three components of sexual behavior.

## 2. Materials and methods

### 2.1. Animals

We used first and second generation laboratory born meadow voles descended from individuals captured at the Miami University Ecological Research Center (Oxford, OH, USA). Voles were maintained from birth under a long-photoperiod (14:10 h L:D, lights on at 0700 h Central Standard Time (CST). At 21 days of age voles were weaned and housed with littermates in clear plastic cages (26 × 32 × 31 cm; *l*, *w*, *h*, respectively) containing wood chip bedding and cotton nesting material. We changed cotton nesting material and hardwood shavings weekly. At 42 days of age, animals were separated from littermates and singly housed in clear plastic cages (27 × 16.5 × 12.5 cm; *l*, *w*, *h*, respectively) unless otherwise noted. Voles born and reared in long-photoperiod reach puberty between 50–60 days of age [22]. We used male voles that were 90–150 days old and not previously food-deprived. Males were sexually experienced, having previously sired a litter. We also used female voles that were 80–150 days old, sexually naïve, and not previously food-deprived. Female meadow voles do not undergo estrous cycles and those born and reared under a long-photoperiod (please see above) readily mate when paired with long-photoperiod male conspecifics [22].

### 2.2. Food deprivations

We weighed female voles 24 h before they were used in the experiment. By doing so, we were able to assign female voles to treatment groups (see below for further details) using a randomization procedure based on body weight. Thus, we insured that female body weight was normally distributed across all treatment groups. Next, female voles were assigned to a group that had continuous access to food (*ad lib*-fed, AL) or to one of the groups that were food-deprived for different intervals. Females in the *ad lib*-fed group received Purina Rodent Diet # 5008 (PMI Inc., St. Louis, MO, U.S.A.) and water. Females in the food-deprived groups received only water; we removed all the food from their cage tops and from the floor of their cages. Female voles that were food-deprived were without food for either for 0 h, 6 h, 12 h, or 24 h. Females that were food-deprived for 6 h (FD 6) underwent tests for proceptivity and receptivity, whereas those that were food-deprived for 12 h (FD 12) and 24 h (FD 24) underwent tests for attractivity, proceptivity, and receptivity. Females that were food-deprived for 6 h did not undergo attractivity tests because this interval was not sufficient to reduce the attractiveness of their odors to male conspecifics [22]. Female voles were food-deprived only once and returned to their home cages after testing. The University of Memphis Institutional Animal Care and Use Committee approved all procedures, and all procedures followed the guidelines set forth by the National Institutes of Health.

### 2.3. Experiment 1

Is acute food deprivation sufficient to lower circulating titers of estradiol of female voles?

#### 2.3.1. Procedure

We food-deprived female voles for 0 h (*ad lib*-fed), 6 h, 12 h, or 24 h intervals as described above. When the females had been food-deprived for the designated interval, we anesthetized each one with isofluorane vapors and obtained a blood sample via cardiac puncture. All sampling took place between 0800 and 0900 CST. We analyzed the plasma samples via enzymatic immunoassay (EIA) using estradiol assay kits from Diagnostic