Physiology & Behavior, Vol. 36, pp. 17–23. Copyright © Pergamon Press Ltd., 1986. Printed in the U.S.A. 0031-9384/86 $3.00 + .00

Infanticide and Parental Behavior in Wild Female House Mice: Effects of Ovariectomy, Adrenalectomy and Administration of Oxytocin and Prostaglandin $F_2\alpha$

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Received 19 February 1985

McCARTHY, M. M., J. E. BARE AND F. S. VOM SAAL. *Infanticide and parental behavior in wild female house mice: Effects of ovariectomy, adrenalectomy and administration of oxytocin and prostaglandin $F_2\alpha$.* PHYSIOL BEHAV 36(1) 17–23, 1986.—We have previously observed that about 60% of virgin, wild female house mice (*Mus musculus*), that were the offspring of wild mice trapped in Missouri, exhibited infanticide when a single 2-day-old pup was placed into each female's home cage. But, by the end of pregnancy, there was a significant increase (to 90%) in the proportion of wild female mice that exhibited infanticide. At parturition, infanticide was inhibited and parental behavior was induced in all females. In the present study we examined the influence of ovarian and adrenal hormones, as well as two hormones associated with pregnancy and parturition: oxytocin and prostaglandin $F_2\alpha$ (PGF), in regulating infanticide and parental behavior in wild female house mice. The presence or absence of gonadal and adrenal hormones did not influence the frequency of infanticidal behavior in adult female mice. Subcutaneous injections of either oxytocin or PGF inhibited infanticide in previously infanticidal pregnant females 1 hr after injection, but only oxytocin served to also facilitate parental behavior (most PGF-treated females left the pup untouched). Oxytocin, but not PGF, was effective in inhibiting infanticide in previously infanticidal virgin females. These findings suggest that, by themselves, ovarian and adrenal hormones do not mediate the exhibition of infanticide by wild female mice, but the lack of response to PGF in virgin females suggests that endocrine changes during pregnancy (possibly changes in steroids) may modulate the inhibitory effects of PGF on infanticide.

Infanticide Maternal behavior Parental behavior Female mice Ovariectomy Adrenalectomy Oxytocin Prostaglandin Pup-killing

INFANTICIDE in house mice has traditionally been considered to be an androgen-dependent behavior exhibited by males and only rarely by females [34,37]. Recently, however, it was reported that most (90%) of the female offspring of wild house mice trapped in Israel were infanticidal as virgins [11]. We have observed that the frequency of infanticide in the female offspring of wild house mice (referred to as "wild-type" mice) trapped in Missouri varies depending on reproductive status: of 83 virgin females tested, 61% were infanticidal. But, significantly more (90%) of the females were infanticidal during late pregnancy. In contrast, these same females exhibited normal parental behavior toward both their own and unfamiliar pups after parturition [16].

Previous studies on infanticide in domestic stocks of house mice have found the frequency of infanticide to be higher in prepubertal than in adult females [35]. However, our findings with wild-type female mice were quite different. We found that the frequency of infanticide was significantly lower in prepubertal females (33% were infanticidal) than in adult virgin females [16]. In addition, our finding that the frequency of infanticide increased during late pregnancy in wild-type female house mice was in contrast to previous studies using domestic stocks of rats and mice in which the onset of some aspects of maternal behavior has been correlated with advancing gestation [21, 27, 29]. We have observed that infanticide in wild-type female house mice was only inhibited around the time of parturition. In the present experiments we sought to determine: (1) whether adrenal and gonadal steroids were required for female mice to exhibit infanticide and (2) what mechanisms might be responsible for the observed changes in infanticidal behavior at parturition.

GENERAL METHOD

Wild house mice (*Mus musculus*) were trapped using

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Sherman live traps in an abandoned building in a field on the Charles W. Green Experimental and Research Wildlife Management Area located in Boone County, Missouri. Approximately 100 wild mice were originally trapped (roughly 40 males and 60 females) and were then bred in a closed colony in which no brother-sister matings were allowed. The animals utilized in the experiments were the F_1–F_4 offspring of the mice wild-trapped in the field. These animals are referred to as wild-type mice since about 20% of the pairs of wild-trapped mice did not produce young. Matings were obtained with one male and one female per cage. All animals were weaned at 25 days of age and then housed in same-sex groups. The mice were housed in rooms maintained at 23±1°C on a 12:12 light:dark cycle, with lights on at 0600 hours. Housing consisted of polypropylene cages (18×29×13 cm) with aspen bedding. Purina breeder chow and water were available ad lib.

All females to be tested were naive (they had no previous experience with pups), and they were isolated for 5 days prior to testing. When a female was tested, one 2-day-old pup was quietly placed into the corner of her cage, and the animals were left undisturbed for 30 min. If a female was found in the nest hovering over the pup, the behavior was recorded as "parent." If the pup was found dead, the behavior was recorded as "infanticide," and if the pup was cold, unharmed, and not in a test female's nest, the behavior was recorded as "untouched." We did not determine whether a pup had actually been left completely untouched by a test animal, but only those animals that could be positively confirmed as exhibiting infanticide or parental behavior were classified accordingly. In these experiments we utilized a 30-min test period without direct observation due to concerns that closely monitoring the behavior of the females might alter their behavior.

The pups used in these experiments were 2-day-old CF-1 albino pups. We have observed that neither wild-type male nor female mice in our colony behave differently toward CF-1 and wild pups. We are not suggesting that adult mice cannot discriminate between albino and wild-type pups (in fact, there is evidence for pup discrimination by lactating mice; [6]). But, whether an adult mouse exhibits infanticide or parental behavior does not appear to be influenced by the characteristics (strain, sex or age) of the young (cf. [11, 14, 16, 34, 36, 40, 41]).

RESULTS

1. Effect of Ovariectomy and Adrenalectomy on Infanticide by Adult Virgin Females

Virgin female wild-type house mice, 70–90 days old, were pretested for infanticidal behavior (see [16]). Only females that exhibited infanticide (approximately 60%) were utilized in this study. Bilateral ovariectomies were performed on 25 infanticidal females under nembutal anesthesia. The females were housed individually after surgery. The previously infanticidal females were tested for infanticide 5 days later, and 88% remained infanticidal after ovariectomy.

Fourteen of the females that remained infanticidal after ovariectomy were subsequently adrenalectomized 2 weeks after ovariectomy using nembutal anesthesia. In addition, 14 previously infanticidal virgins with intact ovaries were adrenalectomized. The adrenalectomized animals were given 1% NaCl and 0.5% dextrose in their drinking water. The females were tested for infanticide 5 days after surgery, and then the absence of adrenal tissue was verified in all females at autopsy.

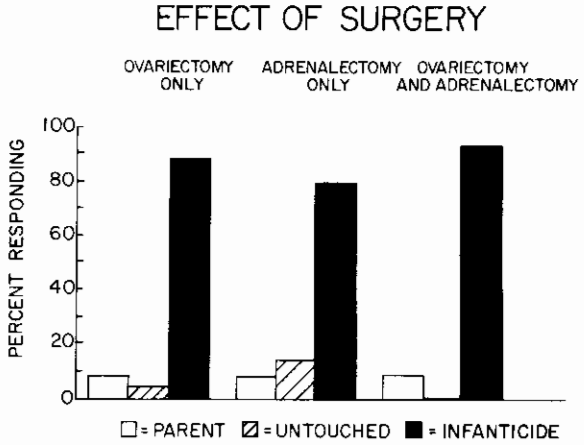

FIG. 1. The percent of wild-type female house mice (that had exhibited infanticide on a pre-test prior to surgery) that exhibited infanticide, parental behavior, or left untouched a single 2-day-old pup that was placed into each female's home cage for 30 min. The females were examined 5 days after surgery to determine whether their behavior toward young would change after ovariectomy (N=25), adrenalectomy (N=14), or ovariectomy and adrenalectomy (N=14).

Neither adrenalectomy nor ovariectomy and adrenalectomy influenced the incidence of infanticide in female mice; 79% of the adrenalectomized virgins with intact ovaries exhibited infanticide, and 93% of the ovariectomized and adrenalectomized virgins exhibited infanticide when tested 5 days after surgery (see Fig. 1). Again, all of these females had exhibited infanticide on the pretest, and the removal of steroid-secreting organs did not result in a significant decrease in the frequency of infanticide in these females (few infanticidal virgin females change in their behavior toward young when retested; see Experiment 5 below).

2. The Behavior Toward Young of Ovariectomized-Adrenalectomized Females Without Prior Experience Exhibiting Infanticide

Most naive, domestic male house mice do not exhibit infanticide following gonadectomy [34, 35, 37]. But, if male mice have been given the opportunity to exhibit infanticide, gonadectomy does not result in a significant decrease in the tendency for male mice to exhibit infanticide, although this conclusion was based on a small sample [10]. In order to determine whether the experience of exhibiting infanticide during the pretest in the prior experiment resulted in an uncoupling of the influence of steroid hormones on the behavior of female mice toward young, 10 naive females were ovariectomized and adrenalectomized using the same surgical procedure described above. The mice were then tested for infanticide 5 days after surgery. There was no difference in the frequency of infanticidal behavior between naive, intact virgins (61% exhibited infanticide, 15% exhibited parental behavior, and 24% left the pup untouched [16]) and the ovariectomized and adrenalectomized virgin females (60% exhibited infanticide, and 40% left the pup untouched) (χ^2, $p>0.1$). Therefore, ovariectomy and/or adrenalectomy do not influence the behavior of virgin female house mice toward young regardless of whether or not the females have had the experience of previously exhibiting infanticide.

3. The Effect of Ovariectomy on Changes in Behavior Toward Young During Adolescence in Female Mice

There is a significant increase in the frequency of infanticide during adolescence in wild-type female mice [16]. To determine if ovarian secretions during adolescence influence infanticidal behavior in adulthood, 22 female mice were bilaterally ovariectomized as juveniles (between 40–42 days old and prior to vaginal opening) using nembutal anesthesia. Following surgery the mice were housed individually for 2 weeks and then group-housed 5 per cage until 5 days prior to testing. The testing procedure was the same as that previously described, and testing occured when the mice were fully mature at approximately 70 days of age.

Of the 22 prepubertally-ovariectomized females tested, 59% exhibited infanticide, 9% behaved parentally, and 32% left the pup untouched. Thus, there is no significant difference in the frequency of infanticide by prepubertally-ovariectomized, adult virgin females and the intact, adult virgin females tested previously ([16]; χ^2, $p>0.1$).

4. Effect of Treatment With Oxytocin or Prostaglandin on Infanticide by Pregnant Females

Adult female wild-type house mice were housed for 2 weeks with a stud male, after which the male was removed. Females that were visibly pregnant were pretested for infanticide. Only infanticidal females were utilized in the subsequent experiment. After the pretest the mice were left undisturbed for 2 hr, and then 21 previously infanticidal females were given a single subcutaneous 5 USP injection of oxytocin (Med. Tech. Inc., Elwood, KA). In addition, 19 previously infanticidal females were injected subcutaneously with a single 500 μg dose of prostaglandin $F_2\alpha$ (PGF; UpJohn, Kalamazoo, MI). Nineteen previously infanticidal pregnant females were also administered a 0.10 cc injection of physiological saline. The dose of oxytocin utilized was based on the results of a pilot study in which doses of between 2 and 8 USP were administered to pregnant wild-type female mice. The dose of PGF used here was based on doses used by other investigators [3, 5, 26] as well as the results of a pilot study in which up to 1.5 mg of PGF was injected SC into pregnant wild-type female mice. In neither the PGF nor the oxytocin pilot studies did the higher doses result in a different effect on the females' behavior from that reported below.

All mice were left undisturbed for 1 hr after the injection, and then a pup was placed into each female's cage. The response of the test female toward the pup was recorded at hourly intervals for 5 hr. Once a female exhibited infanticide, she was not given another pup, and her behavior was recorded as "infanticide" at all subsequent times. Immediately after the end of the experiment, the pregnant females were sacrificed by cervical dislocation, and the fetuses were weighed to determine the day of pregnancy. A previously established profile of fetal weights on Days 11–18 of pregnancy (gestation lasts 18 days) in time-mated, wild-type females was used as a reference for estimating the day of pregnancy.

Oxytocin-injected, previously-infanticidal, pregnant mice were significantly less likely to exhibit infanticide (2/21) and more likely to exhibit parental behavior (6/21) than were saline-treated controls, 18/19 exhibited infanticide; $\chi^2(2)=21.57$, $p<0.001$; see Fig. 2. The response of oxytocin-injected females toward pups was still significantly different from control females 5 hr after the injection, $\chi^2(2)=20.79$, $p<0.001$. Of the 21 pregnant females injected with oxytocin, 14 were between Days 11–14 of pregnancy and 7 were between Days 15–17 (28.5% and 14% had killed the pup by 5 hr after injection, respectively).

PGF-injected pregnant mice were also significantly less likely to exhibit infanticide than were saline-injected controls, $\chi^2(2)=24.00$, $p<0.001$; see Fig. 3. The effect of PGF was transient in some females, and by the fifth hour after injection, 11 of 17 females had become infanticidal again. However, the behavior of the PGF-injected females 5 hr after injection was still significantly different from that of saline-injected control females, $\chi^2(2)=7.37$, $p<0.05$. At 1 hr after the injection, only 2/19 (11%) of PGF-treated pregnant females exhibited parental behavior. PGF thus inhibited infanticide but did not facilitate parental behavior in pregnant female mice. Of the 19 pregnant females injected with PGF, 8 were between Days 11–14 of pregnancy and 11 were between Days 15–17 of pregnancy (62% and 54% had killed the pup by 5 hr after injection, respectively).

5. Effect of Treatment With Oxytocin or Prostaglandin on Infanticide by Adult Virgin Females

Virgin female wild-type house mice between 70–90 days of age were pretested for infanticide, and only females that exhibited infanticide were used in the following experiment. After the pretest, the females were left undisturbed for 2 hr. Seventeen infanticidal females were injected subcutaneously with a single 5 USP (0.25 cc) dose of oxytocin. Another 17 infanticidal females were injected subcutaneously with a single 500 μg (0.05 cc) dose of PGF. To serve as controls, 16 previously-infanticidal, virgin females were administered a 0.10 cc injection of physiological saline.

All of the females were left undisturbed for 1 hr after the injection and then a single pup was placed into each female's cage. The behavior of each female toward the pup was recorded at hourly intervals for 5 hr, beginning with the behavior exhibited at the time the pup was placed into the cage 1 hr after the injection. Once a female exhibited infanticide, she was not given another pup, and her behavior was recorded as "infanticide" at all subsequent times.

One hour after the injection, previously-infanticidal, virgin females treated with oxytocin were less likely to exhibit infanticide (8/17 exhibited infanticide) and more likely to parent the pup (5/17 exhibited parental behavior) than were previously infanticidal virgin, saline-injected controls, 14/16 exhibited infanticide, 1/16 exhibited parental behavior, and 1/16 left the pup untouched; $\chi^2(2)=6.1$, $p<0.05$, see Fig. 2. The difference between saline and oxytocin-treated females was still statistically significant 3 hr ($p<0.05$) but not 5 hr ($p=0.06$) after the injection.

Infanticidal virgin females injected with PGF did not differ in their response toward pups from saline-injected controls: 16/17 PGF-treated females exhibited infanticide immediately after the pup was placed into the cage 1 hr after injection, while 1 female left the pup untouched throughout the test period (see Fig. 3). Since virtually all saline-treated and PGF-treated females exhibited infanticide as soon as the pup was placed into their cages 1 hr after injection, a statistical comparison was only made at this one time point.

6. Effect of Vaginal Stimulation on Infanticide by Pregnant Female Mice

In this experiment we sought to determine if stimulation of the cervix and vagina of a pregnant female mouse might mimic the mechanical events of parturition and thereby in-

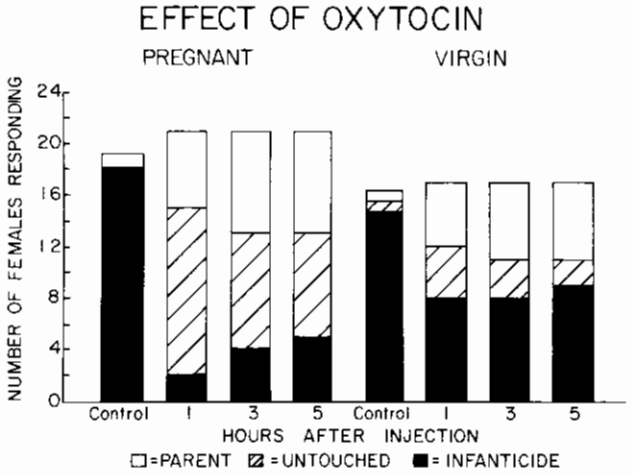

FIG. 2. The number of pregnant and virgin wild-type female house mice that exhibited infanticide, parental behavior, or that left a single 2-day-old pup untouched after a single subcutaneous injection of oxytocin. Only females that exhibited infanticide on a pre-test on the morning of the experiment were utilized. A single 2-day-old pup was placed with each female 1 hr after hormone injection, and the response at 1, 3 and 5 hr for the oxytocin-treated females and at 1 hr for the saline-treated controls is presented.

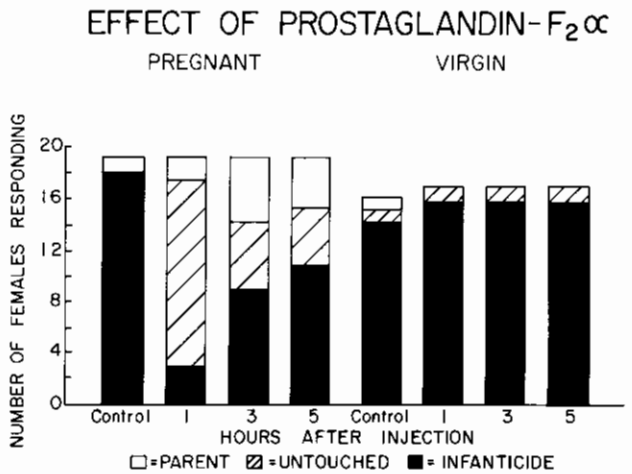

FIG. 3. The number of pregnant and virgin wild-type female house mice that exhibited infanticide, parental behavior, or that left a single 2-day-old pup untouched after a single subcutaneous injection of prostaglandin $F_2\alpha$ (PGF). Only females that exhibited infanticide on a pre-test on the morning of the experiment were utilized. A single pup was placed with each female 1 hr after the hormone injection, and the animals were examined at hourly intervals. The response at 1, 3 and 5 hr for PGF-treated females and at 1 hr for saline-treated controls is presented.

hibit infanticide. Eleven wild-type females that were between Day 15 and Day 18 of pregnancy were stimulated by inserting a metal probe into the vagina and touching the cervix on at least 10 separate thrusts. The females were then returned to their cages and tested for infanticide 1 hr later. If mechanical stimulation of the cervix were to mediate the inhibition of infanticide at parturition, then an interval of 1 hr between stimulation and exposure to a pup should be sufficiently long, since with latencies of even 1 hr, most of the litter would be killed. Ten (91%) of the vaginally-stimulated females exhibited infanticide, and this frequency of infanticide is not significantly different from previously examined [16], unhandled pregnant females (90% were infanticidal; χ^2, $p>0.1$). The day of testing was calculated based on the day of delivery, which is Day 18 of pregnancy for wild-type females. Four females were tested on Day 15, 2 females were tested on Day 16, 3 females were tested on Day 17 (1 of these females left the pup untouched), and 1 female was tested on day 18 of pregnancy (a few hours prior to parturition). Since the blood concentrations of numerous hormones change dramatically during the last 4 days of pregnancy in mice [38], and some females were tested on each of the last 4 days of pregnancy, these negative results are not likely to be due to a failure to provide vaginal stimulation against the proper endocrine background. Thus, either the experimental technique did not accurately mimic the mechanical events of parturition, not enough stimulation was received by the females, or vaginal stimulation is not a significant factor in inhibiting infanticide and inducing parental behavior in pregnant female mice.

DISCUSSION

In one strain of domestic mice (C57BL/6J), more adult females that were gonadectomized either at birth or at 25 days of age have been reported to exhibit infanticide than gonadally-intact adult females using the same procedure to test for infanticide that is described in the present paper. There was also a decrease in the proportion of C57 female mice that exhibited infanticide during adolescence. These findings had led to the suggestion that gonadal steroids acted to inhibit infanticide in female mice, but that there was an interaction between hormonal state and genotype in female mice in terms of behavior toward young (since few female mice from the DBA strain exhibited infanticide regardless of age or endocrine state [15,35]).

In wild-type female mice that we have tested for their behavior toward young, about 60% of females have exhibited infanticide whether they were gonadally-intact or were gonadectomized either prepubertally or in adulthood (see also [16]). Adrenalectomy also was without effect on the proportion of wild-type females that exhibited infanticide. Thus, the results of our experiments indicate that in virgin, wild-type female mice, infanticide occurs in the absence of steroid hormones of either ovarian or adrenal origin. Therefore, these results do not support the hypothesis that gonadal and/or adrenal steroids directly mediate either the exhibition or the inhibition of infanticide in virgin, wild female mice.

In most domestic stocks of mice, males are significantly more likely to exhibit infanticide than are females, although differences between domestic stocks in the frequency of infanticide for both males and females have been reported [34,35]. We have observed that in wild-type mice, significantly more sexually-naive males (about 90%) than virgin females (about 60%) exhibit infanticide [16, 17, 18]. It is also well established from studies with domestic stocks of mice that androgen exposure both around the time of birth (prenatal and postnatal) and in adulthood markedly influences the frequency of infanticide in groups of males [34,37]. While these findings appear to support the hypothesis that the relationship between hormones and infanticide in female mice is fundamentally different from that in male mice, in fact, a

recent study suggests that this might not be the case. We have observed that 9 of 10 adult, naive, wild-type male mice exhibited infanticide two weeks following castration when tested with the same procedure described in the present studies. Since the testing procedure that is used has a dramatic effect on the behavior of wild-type male mice toward young [17,18], other wild-type males were also tested by being placed into the cage of a lactating female and her litter 4 weeks following castration, and 7/10 of these castrated males exhibited infanticide (unpublished observation). Taken together with the results of the present experiments, and in marked contrast to studies with outbred domestic stocks of mice, these findings suggest that in wild-type male and female mice, the exhibition of infanticide may be independent of circulating concentrations of gonadal hormones at the time of testing. It is possible, however, that steroids mediate the organization during early life of sex difference in the frequency of infanticide in wild-type mice.

One of the striking features of infanticide in wild-type female house mice is that most previously noninfanticidal females become infanticidal during late pregnancy, but all females then care for their own litters after parturition [16]. These findings contrast with the results of other experiments using domestic stocks of mice and rats [21,29], although there is one study that reports that in Long Evans rats, virtually all virgin females exhibit infanticide. While there was a significant reduction in the proportion of Long Evans females that exhibited infanticide just prior to parturition, many females continued to exhibit infanticide just prior to the birth of their own litters [27]. These findings suggest that in Long Evans rats as well as wild-type house mice, events either very close in time to parturition or during parturition mediate the inhibition of infanticide. Our findings do contrast with the study with rats by Peters and Kristal [27] in that we observed an increase in the proportion of females exhibiting infanticide prior to parturition [16] while they observed a slight, but significant, decrease in infanticide prior to parturition.

There are numerous changes in the endocrine profile of female mice during pregnancy [38] that may be responsible for mediating changes in infanticidal behavior. The current finding that there is no effect of either ovariectomy or adrenalectomy on infanticide argues against the hypothesis that steroid hormones are involved in directly inducing the increase in infanticidal behavior during pregnancy in wild female house mice, although interactive effects with other hormones, such as oxytocin and prostaglandins, are possible. Given the findings with C57 female mice [15,35], it also cannot be ruled out that changes in steroid hormone concentrations during pregnancy (for example, an increase in the concentration of circulating estradiol [2,19]) play a role (again, likely interactive) in mediating the inhibition of infanticide that occurs at parturition in wild-type female mice.

Oxytocin is a peptide hormone that is synthesized in the hypothalamus and secreted from the posterior pituitary into the circulation in response to suckling and vaginal-cervical stimulation [23,32]. As with other peptides once thought to operate only outside the CNS, recent studies have revealed that there is a widespread distribution of oxytocin-containing neurons within the brain [22]. In addition, there is some evidence for the direct release of oxytocin into the cerebrospinal fluid, and it has been proposed that hypothalamic peptides, such as oxytocin, might exert their behavioral effects via direct neural connections [8,31]. Intracerebroventricular administration of oxytocin has been found to induce maternal behavior in ovariectomized, estrogen-primed rats of one domestic stock [9, 23, 24], but not others [4,30].

In the current study we found that a single subcutaneous injection of oxytocin was effective in inhibiting infanticide by pregnant females, and somewhat less effective in inhibiting infanticide by virgin females. There is evidence for oxytocin crossing the blood-brain barrier, and it has been reported that oxytocin injected subcutaneously can be detected in the cerebrospinal fluid within ten minutes of injection [20]. The behavioral changes observed in the present study after a systemic injection of oxytocin thus might have been due to a direct effect of oxytocin on the CNS (after crossing the blood-brain barrier), to stimulation by oxytocin of the release of some other substance, or to stimulation of peripheral sensory receptors (and thus indirectly the brain). Further studies are required to distinguish between central and peripheral effects of oxytocin in wild female house mice.

There was a significant increase in the frequency of parental behavior exhibited by females after an oxytocin injection, although the majority of the pregnant females left the pup untouched. Previous studies have indicated that the biological activity of oxytocin is influenced by the current or prior circulating concentrations of ovarian hormones; intraventricular injections of oxytocin failed to elicit maternal behavior in rats in the absence of prior priming with estradiol [9, 23, 24]. It has been proposed that one of the effects of the rise in estradiol and decrease in progesterone, which occurs in mice [2,19] as well as rats near term, is to increase the sensitivity of uterine and mammary tissues to oxytocin [33]. In this study we found that oxytocin was effective in inhibiting infanticidal behavior in pregnant females (throughout the last week of gestation) as well as in virgin females. These findings suggest that the increase in estradiol and decrease in progesterone near term might not play a major role in modulating the effect of oxytocin in inducing parental behavior and inhibiting infanticide in wild female mice, although further studies to test this hypothesis directly are required.

The biological activity of PGF has been extensively studied with regard to its luteolytic effects as well as its ability to interfere with implantation after conception [3, 5, 25]. Once implantation has occured, administration of PGF can adversely affect the developing embryos [26] and may result in premature parturition [12]. In the present study several of the pregnant females treated with PGF were found at autopsy to have dead fetuses. Therefore, it is possible that the high percentage of PGF-treated pregnant females that left the pup untouched may have been the result of internal physiological events disrupting the normal behavior of the females rather than to the inhibition of infanticide by PGF *per se*.

In the current study subcutaneous administration of PGF was effective in inhibiting infanticidal behavior in previously infanticidal pregnant females but was without effect in previously infanticidal virgin females. There was no significant facilitation of parenting behavior observed in either the virgin or pregnant females receiving the PGF injection, which is in contrast to the facilitation of parental behavior observed in females receiving the oxytocin injection. Furthermore, the inhibition of infanticide after PGF injection decayed faster than after oxytocin injection. In a previous study utilizing rats, prostaglandin administered intraventricularly induced partial maternal behavior that had an early onset but did not persist [23].

It has been reported that both the oviduct and uterine response to PGF is dependent upon the endocrine status of

the animal, in particular, the steroidal environment to which these organs are exposed [12]. Again, we found PGF to be effective in inhibiting infanticide by pregnant females throughout the last 7 days of gestation but to be completely ineffective in inhibiting infanticide in previously infanticidal virgin females. This finding suggests that the endocrine environment of pregnancy is required for PGF to elicit a behavioral response in female mice. The pregnant uterus synthesizes less PGF than either the psuedopregnant or nonpregnant uterus, and it has been proposed that the conceptus inhibits PGF production by the uterus as well [7]. Prostaglandin-metabolizing activity is also high in fetal membranes [11]. Thus, a picture emerges of blood titers of PGF being low in pregnant females compared to virgin females, and then rising again near parturition due to release of the inhibitory effects of pregnancy on PGF synthesis and release. This picture of fluctuating PGF titers correlates well with the frequency of infanticide observed by females in various reproductive states. About 60% of virgin females and 60% of primiparous but nonpregnant and nonlactating females exhibit infanticide as compared to over 90% of pregnant females, but virtually no female mice are infanticidal toward their own litters at parturition [16]. Thus, when PGF titers are at their lowest (during the second half of pregnancy), the frequency of infanticidal behavior is at its highest, and when PGF levels begin to rise (near parturition), infanticidal behavior is inhibited. Therefore, it is possible that the high frequency of infanticide by pregnant female mice is induced by low levels of PGF, and the inhibition of infanticide and appearence of parental behavior at parturition may be the result of increasing PGF titers, as well as oxytocin and other hormones (such as steroids).

A positive interaction between PGF and oxytocin may occur in both the uterus and brain of parturient rats, and PGF may enhance the expulsion of the fetuses while oxytocin triggers the onset of maternal behavior [23]. The data presented here suggest that PGF and oxytocin might also interact to regulate infanticide and parental behavior in female mice. It has been reported that oxytocin results in the release of PGF directly from the uterus and that intraventricular administration of PGF to lactating rats increases the firing rate of oxytocin-containing neurons in the paraventricular nucleus [1]. Similarly, PGF administration might result in the release of oxytocin. Attempting to separate the independent effects of these two hormones on the behavior of female mice toward young is thus not possible based on the present experimental design, and the significance of the finding that oxytocin both induced parental behavior and inhibited infanticide, while PGF only inhibited infanticide in pregnant females, remains to be determined.

There are also physical changes associated with parturition that may play a role in determining the response of a female mouse toward pups. For instance, vaginal stimulation has been found to induce maternal behavior in sheep [13], and vaginal distension results in the release of oxytocin in goats [28]. However, in the current study we found a moderate amount of mechanical stimulation of the cervix of a pregnant female mouse to be without effect on infanticide.

In conclusion, the results of this study indicate that removal of gonadal and adrenal hormones does not influence the exhibition of infanticidal behavior in adult, virgin wild-type female mice, but the occurrence of infanticide by females was influenced by exogenous administration of the hormones oxytocin and PGF. Oxytocin was effective in inhibiting infanticide and facilitating parental behavior in both pregnant and nulliparous wild-type female mice. PGF, on the other hand, was only effective in inhibiting infanticide by pregnant females and did not induce parental behavior in any females.

ACKNOWLEDGEMENTS

This research was conducted in partial fulfillment of the M.A. degree by M.M.M. and was supported by grants to F.v.S. from NINCDS, NIH (NS 20075), NSF (BNS 8203714), and the University of Missouri Research Council (University of Missouri Biomedical Research Support Grant RR 07053 from NIH). We thank Dr. Billy Day for providing the oxytocin and prostaglandin.

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