Amygdala but not hippocampal lesions impair olfactory memory for mate in prairie voles (*Microtus ochrogaster*)

GREGORY E. DEMAS,[1] JOSEPH M. WILLIAMS,[2] AND RANDY J. NELSON[1,3,4]
[1]*Department of Psychology, Behavioral Neuroendocrinology Group,* [3]*Department of Neuroscience, and* [4]*Department of Population Dynamics, Reproductive Biology Division, The Johns Hopkins University, Baltimore, Maryland 21218; and* [2]*Department of Psychology, The Ohio State University, Columbus, Ohio 43210*

Demas, Gregory E., Joseph M. Williams, and Randy J. Nelson. Amygdala but not hippocampal lesions impair olfactory memory for mate in prairie voles (*Microtus ochrogaster*). *Am. J. Physiol.* 273 (*Regulatory Integrative Comp. Physiol.* 42): R1683–R1689, 1997.—Exposure to an unfamiliar male conspecific results in pregnancy interruption (i.e., the Bruce effect) in rodents. Unlike most laboratory rodents, female prairie voles (*Microtus ochrogaster*) are induced into estrus by chemosensory stimuli contained in the urine of male conspecifics while grooming the anogenital (A-G) region of unfamiliar males. Female prairie voles maintain a brief "memory" for the stud male for 8–10 days after mating. Subsequent exposure to the same mate within this 8- to 10-day window does not elicit A-G investigation by the female and pregnancy block does not result. However, exposure to the original male after 10 days evokes A-G investigation and pregnancy block. To determine the neuroanatomic area(s) involved in olfactory memory for mate, female voles received bilateral electrolytic lesions of either the amygdala or hippocampus. Females were subsequently exposed to males for 48 h, separated for 3 days, then reintroduced to their original mate for 24 h. Although pregnancy rate did not differ among the experimental groups, a greater proportion of amygdala-lesioned females displayed pregnancy block when reexposed to their previous mates compared with hippocampal- or sham-lesioned voles. Amygdala-lesioned voles also displayed a greater number of A-G investigations compared with the other groups. Performance on olfactory tests was not impaired. Taken together, these results suggest that the amygdala plays an important role in olfactory memory for mate in prairie voles.

pheromones; vomeronasal organ; Bruce effect; pregnancy block; estrus

MAMMALIAN REPRODUCTION is influenced by several extrinsic factors, including photoperiod, temperature, food quality and quantity, and social stimuli (2, 30). Among various social stimuli, chemosensory cues play a fundamental role in reproductive physiology and behavior in many rodent species (3, 22, 41–43). Rodents have two distinct, well-developed olfactory systems: the main olfactory system and the accessory olfactory system (17). The main olfactory system is specialized for the detection of volatile chemosensory signals (36, 37). The accessory olfactory system, in contrast, is used to detect nonvolatile chemosensory cues and requires the animal to come into direct contact with the substance containing the chemosensory stimulus (e.g., urine) (22, 45). Chemosensory cues, acting on the accessory olfactory system, can trigger neuroendocrine events leading to significant changes in circulating hormone levels (6, 39).

The organization of estrus in prairie voles (*Microtus ochrogaster*) differs in comparison to traditional laboratory species such as rats, mice, hamsters, and guinea pigs. Isolated female prairie voles never undergo spontaneous cycles of vaginal cytology, vaginal patency, uterine mass, or behavior characteristic of the estrous cycles of traditional laboratory rodents (35). Instead, female prairie voles must interact with male conspecifics to be induced into estrus. An androgen-dependent component of male urine seems to be necessary and sufficient to induce estrous behavior in the recipient female (28, 29). If females do not engage in anogenital (A-G) investigation and do not come into direct contact with male urine, they are not induced into estrus (5, 14). Females typically engage in A-G investigation with unfamiliar males. Siblings, fathers, or other familiar males are rarely investigated and do not induce estrus, although urine taken directly from familiar males and applied to the nares of females stimulates estrus (5). A behavioral mechanism (i.e., the lack of A-G investigation toward familiar males) prevents females from investigating familiar males and subsequent estrus induction. A familiar male becomes unfamiliar after a minimum period of physical separation lasting 8–10 days in prairie voles (29) and >30 days in house mice (19). These results suggest that females form a memory for their previous mate (1, 22).

A well-studied reproductive phenomenon involving the action of chemosensory cues on estrous behavior is the interruption of gestation when pregnant females are exposed to unfamiliar males (i.e., Bruce effect) (3). After exposure to an unfamiliar male, the female will abort her pregnancy and return to an estrous state within 48 h (4, 7, 8, 32). Exposure to soiled bedding of unfamiliar males alone is sufficient to produce the Bruce effect in mice (4, 10). This phenomenon is not restricted to mice, as it has been demonstrated in several other rodent species including deer mice (*Peromyscus maniculatus*) (13), collared lemmings (*Dicrostonyx groendlandicus*) (27), meadow voles (*Microtus pennsylvanicus*) (23), and prairie voles (*Microtus ochrogaster*) (16, 20). Pregnancy block has been demonstrated in natural and semi-natural environments and therefore is not considered to be merely a laboratory artifact (16).

Pregnancy block is a consequence of hormonal changes due to chemosensory stimuli released by males acting on the female accessory olfactory system. In the accessory olfactory system, nonvolatile chemosensory

stimuli are taken into the external nares via the pumping action of the vomeronasal organ (VNO) (18, 45). From the VNO, a neural signal is sent directly to the medial amygdala (1). From the amygdala, projections are sent to the bed nucleus of the stria terminalis (BNST), the medial preoptic area, the anterior hypothalamus, and the ventromedial hypothalamus (22). In the hypothalamus, the neural signal in response to chemosensory stimulation activates tuberoinfundibular dopaminergic neurons, causing them to secrete dopamine into the hypophysial portal circulation (22). The increase in hypothalamic dopamine causes a decrease in prolactin and a concomitant increase in gonadotropin-releasing hormone (GnRH) secretion. When prolactin concentrations drop, the corpus luteum stops producing progesterone, the blastocyst fails to implant on the uterine wall, and pregnancy is terminated (34). Stimulation of GnRH neurons in the hypothalamus increases secretion of GnRH and subsequent release of luteinizing hormone (LH) by the anterior pituitary. High LH concentrations return the animal to an estrous state (9). Chemosensory stimuli of unfamiliar males stimulate the VNO, activating a neural and hormonal cascade resulting in termination of pregnancy. 6-Hydroxydopamine lesions of the noradrenergic connections from the VNO to the accessory olfactory bulb prevent pregnancy block in house mice (23). Lesions of the VNO also prevent pregnancy block, but leave olfactory discrimination for the smell of urine intact (26).

The amygdala, a relay station for accessory olfactory information, also mediates social behavior in both rodents (24) and nonhuman primates (25). For example, specific nuclei of the amygdala are involved in affiliative behavior in prairie voles; lesions of these nuclei decrease affiliative behavior (24). In rats, the amygdala is a critical structure in memory in both gustatory (21) and early associative olfactory conditioning (41) paradigms. The amygdala interacts with the hippocampus via direct neural projections. Hippocampal lesions produce rapid forgetting of olfactory memory (11, 31–40). However, bilateral hippocampal lesions (i.e., the ventral subiculum and lateral entorhinal cortex) do not affect olfactory memory in mice in the context of pregnancy block (38). Infusions of a local anesthetic into the medial amygdala also fail to disrupt memory for the familiar male (18).

No study, however, has assessed the effects of bilateral electrolytic lesions to either the amygdala or the dorsal and ventral hippocampus on olfactory memory for a mate. If either the amygdala or hippocampus mediates olfactory memory for familiar males, then bilateral ablation of the amygdala should impair this memory and females should exhibit increased A-G investigation toward familiar males after a brief separation compared with controls. The present study was designed to examine the role of the amygdala and hippocampus in pregnancy block in prairie voles.

MATERIALS AND METHODS

Housing conditions. Female prairie voles (*Microtus ochrogaster ochrogaster*) were obtained from a breeding colony within our laboratory. The colony was originally derived from a wild population trapped near Urbana, IL (latitude 40.1° North). All animals were individually housed in propylene cages in colony rooms with a 16:8-h light-dark cycle [lights on at 0600 Eastern Standard Time (EST)]. Temperature was held constant at 20 ± 2°C while relative humidity was held constant at 50 ± 5%. Food (Agway, Prolab 2000) and tap water were provided ad libitum throughout the course of the experiment.

Experimental conditions. Animals were randomly assigned to one of three experimental groups: *1*) animals subjected to bilateral amygdala lesions (n = 22), *2*) animals subjected to bilateral hippocampal lesions (n = 25), and *3*) animals receiving sham surgeries (n = 15). On the basis of preliminary evidence that amygdala lesions disrupted memory for mate, a fourth group (n = 15) was added in which female voles were given bilateral amygdala lesions, paired with a conspecific male for 48 h, and then killed 7 days later. Animals in this last group (amygdala control) were never reintroduced to any male. This group was included to determine whether amygdala lesions alone disrupt estrus induction or pregnancy independently of the reintroduction of the male.

Surgeries. Bilateral electrolytic lesions were performed on animals anesthetized with a ketamine cocktail consisting of ketamine (50 mg/kg), rompun (5 mg/kg), and acepromazine (5 mg/kg). Lesions were conducted with a stainless steel positive electrode (0.25 mm in diameter insulated with epoxylite except for a 0.5-mm portion of the tip). Amygdala lesions were made using the following stereotaxic coordinates: 1.8 mm posterior to bregma, ±3.1 mm lateral to midline, and 4.3 mm ventral to the skull. Animals within the hippocampal group received both dorsal and ventral hippocampal lesions. Dorsal hippocampal lesions were made using the following stereotaxic coordinates: 2.2 mm posterior to bregma, ±2.2 mm lateral to midline, and 2.7 mm ventral to the skull. Ventral hippocampal lesions were made using the following stereotaxic coordinates: 2.7 mm posterior to bregma, ±3.1 mm lateral to midline, and 3.7 mm ventral to skull. A direct current (2 mA; Grass model LM4 lesion maker) was applied at each electrode placement site for 12 s. Control animals received sham surgeries in which small holes were drilled in the skull but the electrode was not lowered into the brain. Three amygdala-lesioned, four hippocampal-lesioned, one sham-lesioned, and two amygdala control voles died during the surgery.

Procedures. All animals were given a postoperative recovery period lasting 7 days after their respective surgeries. After recovery, they were placed in separate glass vivaria containing clean bedding, food, and water. After a 10-min acclimation period, a single conspecific male was introduced into the vivarium. They were housed in this condition for 48 h to allow the formation of olfactory memory between the animals. The animals were filmed during this period to determine if mating occurred. The females were then separated from the male and placed individually in fresh propylene cages. After 3 days, the females that had originally mated were reintroduced to the same male. This was done by placing the female back into a fresh vivarium, allowing a 10-min acclimation period, and then reintroducing the same stud male previously housed with the female. The animals were filmed in the vivaria for a 24-h period, after which the female was removed and given a lethal dose of pentobarbital sodium.

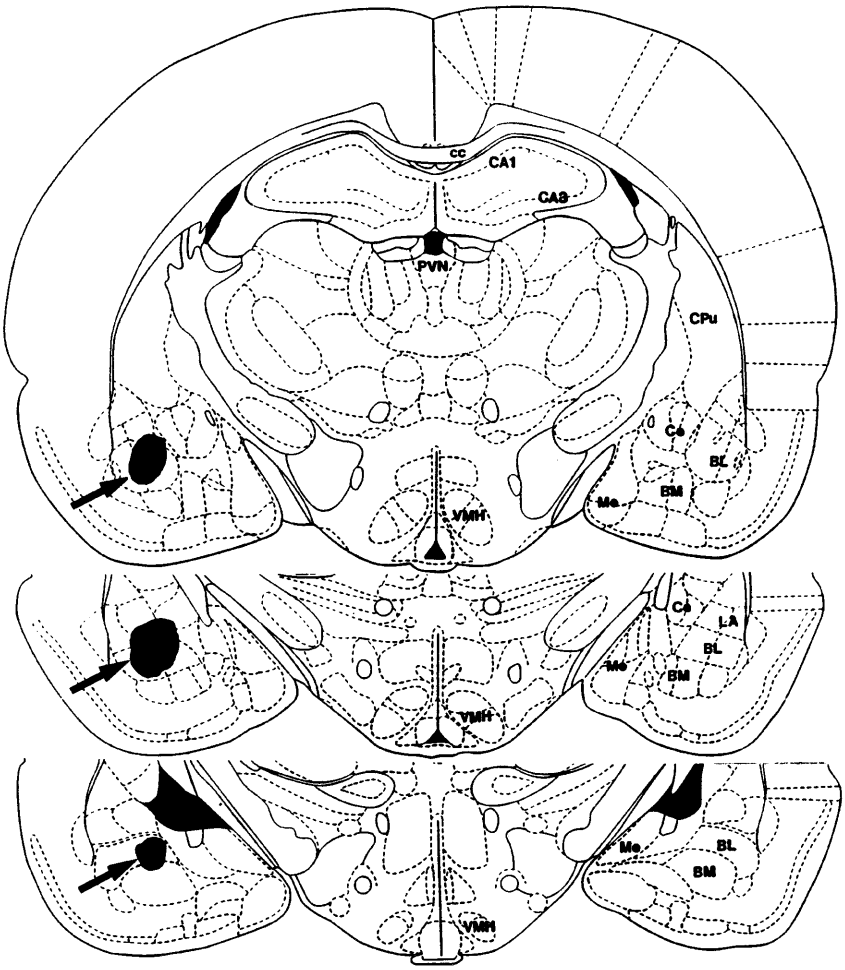

Fig. 1. Representative lesion of amygdala-lesioned prairie voles (arrows). Pictures of lesions were traced from projected images onto drawings (taken from Ref. 33). Lesions were bilateral, but, for purposes of clarity, only 1 representative side is shown. CPu, caudate putamen; cc, corpus collosum; Ce, central amygdala; BM, basomedial amygdala; BL, basolateral amygdala; LA, lateral amygdala; Me, medial amygdala; PVN, paraventricular nucleus; VMH, ventromedial hypothalamus. CA1, field CA1 of hippocampus; CA3, field CA3 of hippocampus.

Behavioral assessment. A-G investigative behavior was assessed by counting the number of A-G investigations occurring in the first 10 min of each hour across the 24-h filming period. Female prairie voles consistently make a greater number of A-G investigations of novel as opposed to familiar males. Because the majority of the A-G investigations occurred within the first 4–5 h after repairing, only these data were used in subsequent analyses. The videotapes were scored by independent coders naive to the experimental conditions. Animals that did not mate were excluded from all subsequent data analyses.

Autopsies. After videotaping, the animals were given a lethal dose of pentobarbital sodium and uterine horns were removed and cleaned of fat and connective tissue. The presence or absence of developing fetuses or implantation sites was recorded to determine if the females had become pregnant. Brains were removed, postfixed, and cryoprotected in a 4% paraformaldehyde (pH 7.5) and 30% sucrose solution. Brain tissue was sliced (40 μm) and stained with cresyl violet to assess lesion accuracy. Animals with lesions missing the targeted areas were excluded from subsequent data analyses. Six amygdala-lesioned animals, seven hippocampal-lesioned animals, and three amygdala control animals were removed because of misguided lesions.

Test of the main olfactory system. In a separate control experiment, the integrity of the main olfactory system was assessed in amygdala-lesioned ($n = 8$) and sham-lesioned animals ($n = 5$). A small piece of cookie (~3 g) was randomly buried in a clean cage with a fresh layer of bedding material (~1-cm deep) covering the bottom. The animal was then placed in the cage and the time required to uncover the cookie was determined. The test was terminated if the animal failed to uncover the cookie within 10 min. Brains were removed and lesion accuracy was assessed as described above. Three amygdala-lesioned animals were removed from the study because of misguided lesions.

Test of the accessory olfactory system. To determine if amygdala lesions affected the accessory olfactory system, an estrus induction test was performed on the same set of animals used in the previous olfactory test. Urine was collected from conspecific males. Two drops of urine were placed directly on the nares of the test females at 1400 EST each day across 4 consecutive days. All animals were then administered a lethal dose of pentobarbital sodium and their uterine horns were removed, cleaned of fat and connective tissue, and weighed. Brains were removed and lesion accuracy was assessed as described above.

Data analyses. The data for A-G investigation were analyzed using a two-way mixed model analysis of variance (Systat). Planned comparisons were conducted between pairwise means. Pregnancy data were analyzed using a one-tail χ^2 test. Data from olfactory tests were analyzed using independent Student's *t*-tests (Systat). Differences between group means were considered statistically significant at $P < 0.05$.

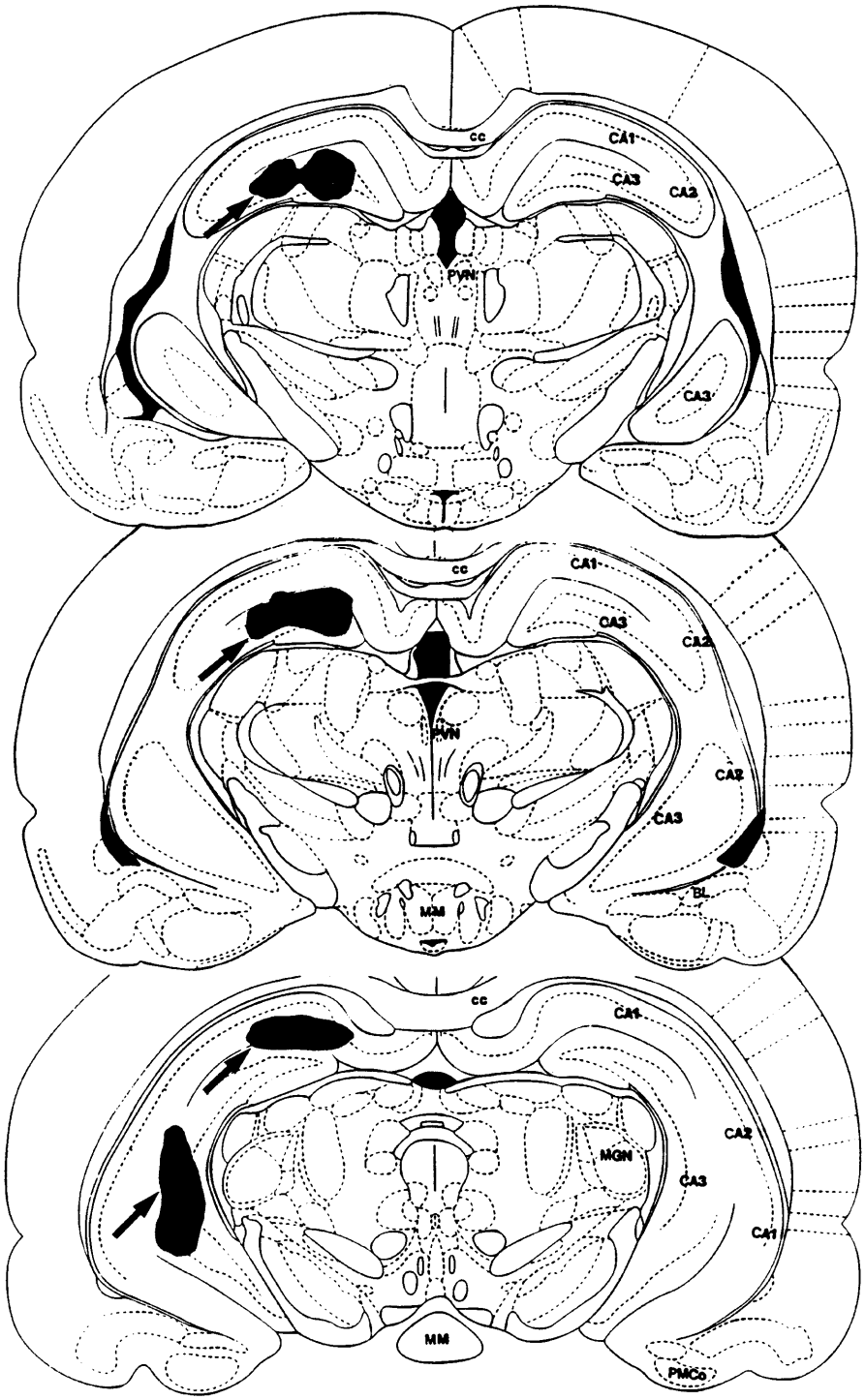

Fig. 2. Representative lesions of dorsal and ventral hippocampal-lesioned prairie voles (arrows). Pictures of lesions were traced from projected images onto drawings (taken from Ref. 33). Lesions were bilateral, but, for purposes of clarity, only 1 representative side is shown. MGN, medial geniculate nucleus; MM, medial mamillary nucleus; PMCo, posteromedial cortical nucleus. CA2, field CA2 of hippocampus.

RESULTS

Representative dorsal and ventral and amygdala lesions are shown in Figs. 1 and 2. Amygdala-lesioned animals showed extensive damage to the basolateral, basomedial, and central amygdala (Fig. 1). Damage did not extend to the medial amygdala, an important relay station for olfactory information that is also part of the neuroendocrine pathway involved in pregnancy block. Moderate lesions were made to the dorsal and ventral subiculum in hippocampal-lesioned animals (Fig. 2).

A similar proportion of animals with amygdala (10/13), hippocampal (11/14), or sham lesions (10/14), and amygdala control animals (8/10) mated during the initial pairing ($P > 0.05$). Of the animals that mated, a

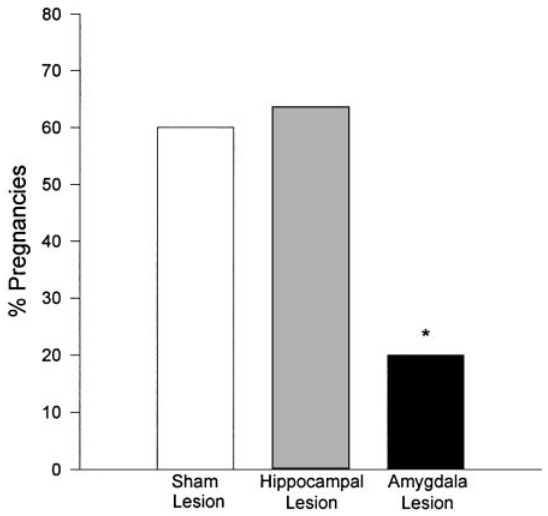

Fig. 3. Percentage of pregnancies among female prairie voles receiving, sham, amygdala, or hippocampal lesions. *Statistically significant differences between groups.

greater proportion of amygdala-lesioned females displayed pregnancy block compared with hippocampal- or sham-lesioned females ($P < 0.05$). Two of ten of the amygdala-lesioned animals that had mated were impregnated, whereas 7 of 11 of the hippocampal-lesioned animals and 6 of 10 of the sham-lesion animals that had mated were impregnated (Fig. 3). There was no difference in the proportion of pregnant voles between amygdala-lesioned voles that were never reintroduced with their mates (i.e., amygdala controls) and either hippocampal- or sham-lesioned voles ($P > 0.05$ in both cases). Within the amygdala control group, six of eight females were impregnated.

Animals in the amygdala-lesioned group engaged in a greater number of A-G investigations during the first 3 h after reintroduction of the familiar mate compared with control ($P < 0.05$) and hippocampal-lesioned animals ($P < 0.05$) (Fig.4). There was no difference between animals with hippocampal lesions and sham-lesioned animals in the degree of A-G investigation ($P > 0.05$).

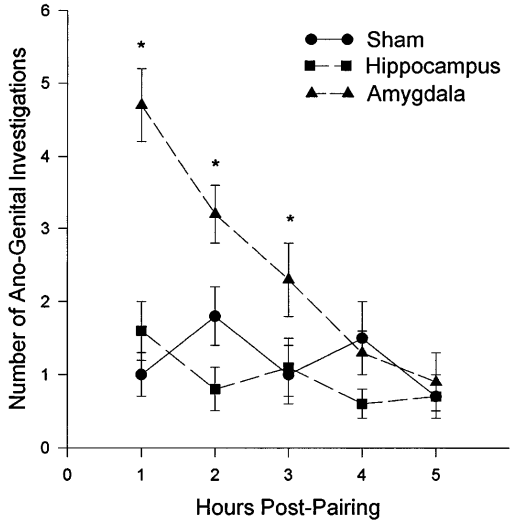

Fig. 4. Mean number of anogenital investigations displayed by female prairie voles receiving sham, amygdala, or hippocampal lesions. *Statistically significant differences among groups.

There were no significant differences between sham- or amygdala-lesioned animals in either of the olfactory control tests ($P > 0.05$ in both cases). In the main olfactory test, the amount of time required to uncover the cookie did not differ between groups (442.0 ± 80.6 s for sham-lesioned voles and 479.3 ± 56.3 s for amygdala-lesioned voles) ($P > 0.05$). In the accessory olfactory test, sham-lesioned and amygdala-lesioned animals did not differ in uterine mass after 4 days of VNO stimulation with male urine (2.61 ± 0.35 mg/g for sham-lesioned voles and 3.23 ± 0.70 mg/g for amygdala-lesioned voles) ($P > 0.05$).

DISCUSSION

Amygdala lesions caused a marked disruption in olfactory memory for mate in female prairie voles (*M. ochrogaster*). In general, amygdala-lesioned voles underwent pregnancy block despite being reintroduced to a familiar male. These animals also displayed greater A-G investigation compared with either hippocampal- or sham-lesioned voles, suggesting that amygdala-lesioned voles failed to recognize their previous mate. These results do not appear to be due to the direct effects of amygdala lesions independent of memory; voles receiving amygdala lesions, but never re-paired with a male, display a comparable proportion of pregnancies to control voles. Although the proportion of females in the control group that mated and became pregnant is low compared with pregnancy rates reported for house mice, this value is typical for prairie voles paired for only 48 h (44).

These data provide the first evidence that the amygdala may play an important role in olfactory memory for mate in the context of pregnancy block in prairie voles. Nonvolatile chemosensory stimuli stimulate the VNO, and the VNO projects directly to the amygdala. The amygdala, in turn, projects to several important neuroanatomic regions, including the BNST, the anterior hypothalamus, and the hippocampus (22). The latter structure plays an important role in memory consolidation (12). Lesions of the hippocampus, however, fail to disrupt olfactory memory for mate (38). The amygdala is involved in olfactory memory and, therefore, is likely to be involved in olfactory memory for mate. The present data are consistent with this hypothesis.

Previous research has suggested that the amygdala does not play a significant role in pregnancy block in house mice (*M. musculus*). For example, infusions of lidocaine into the medial amygdala do not disrupt olfactory memory for mate in this species (18). The apparent discrepancy between these results and those of the present study may be due to differences in methodology and the site of disruption. It is possible that infusions of lidocaine that anesthetize neural tissue and reduce brain activity may not sufficiently

disrupt neural firing within the amygdala compared with electrolytic lesions. Furthermore, the electrolytic lesions used in the present study were generally restricted to the basolateral and central amygdala, whereas the lidocaine infusions described in the previous study were aimed at the medial amygdala. It is possible that the medial amygdala does not play an important role in olfactory memory for mating partner. One common limitation of electrolytic lesions is that, in addition to damaging the targeted neuroanatomic areas, some unintended damage can result due to the lowering of the electrode through the brain. It is possible that some of the results are due to the destruction of fibers of passage to and from the amygdala and not amygdala itself. Further studies using chemical lesion techniques can address this issue.

At the ultimate level of analysis, there likely exists species differences in the neuroanatomic circuitry underlying olfactory memory for mate. Prairie voles, unlike most rodents including mice and rats, are monogamous, forming long-lasting pair bonds with their mate (15). For the female to maintain a pair bond for any extended time (e.g., when the male is away foraging for food), she must remember her previous mate. In contrast, house mice are polygynous, with males mating with many females throughout the reproductive season (2). Thus female mice need not maintain any memory for their previous mate, as they rarely encounter the same male again in the wild. Due to these differences in life history strategies between voles and mice, different neuroanatomic circuits likely have evolved. The increased demand for memory for mate among monogamous individuals may have led to the evolution of more sophisticated neural circuits underlying this type of memory.

Although the present study implicates the amygdala in olfactory memory for mate in female prairie voles, the precise role of this brain region in this phenomenon is not known. The amygdala appears to be an important processing station of olfactory memory within the accessory olfactory system; however, it is only one of many structures within this system. The amygdala likely acts as a processing center of incoming olfactory information rather than being the sole site for olfactory memory. Thus the amygdala may be one link in a complex circuit underlying olfactory memory for mate; other neuroanatomic structures may play equally important roles. An interesting possibility is that the amygdala is involved in the formation but not maintenance of olfactory memory. If true, then lesions occurring after pair bonding has occurred should not affect olfactory memory. Alternatively, if the amygdala is involved in maintenance of olfactory memory, then lesions occurring either before or after pair bonding should disrupt this memory. Further studies need to be conducted to test these hypotheses.

We thank Camron Johnson, Jack Chiang, Sue Yang, Joyce Hairston, Violette Renard, and John Dunlop for technical support. We also thank Sabra Klein and Lance Kriegsfeld for useful suggestions and Dr. Bert Green for statistical advice. We are also grateful to Rick Vagnoni for expert animal care.

This study was supported by National Institute of Mental Health Grant MH-57535 (formerly NICHD-22201).

Address for reprint requests: G. E. Demas, Dept. of Psychology, Behavioral Neuroendocrinology Group, The Johns Hopkins Univ., Baltimore, MD 21218–2686.

Received 15 May 1997; accepted in final form 6 August 1997.

REFERENCES

1. **Brennan, P., H. Kaba, and E. B. Keverne.** Olfactory recognition: a simple memory system. *Science* 250: 1223–1226, 1990.
2. **Bronson, F. H., and P. D. Heideman.** Seasonal regulation of reproduction in mammals. In: *The Physiology of Reproduction* (2nd ed.), edited by E. Knobil and J. D. Neill. New York: Raven, 1994, p. 541–584.
3. **Bruce, H. M.** An exteroceptive block to pregnancy in the mouse. *Nature* 184: 105, 1959.
4. **Bruce, H. M., and D. M. V. Parrot.** Role of the olfactory sense in strange males. *Science* 131: 1526, 1960.
5. **Carter, C. S, L. L. Getz, L. Gavish, L. McDermott, and P. Arnold.** Male-related pheromones and activation of female reproduction in the prairie vole (*Microtus ochrogaster*). *Biol. Reprod*. 23: 1031–1038, 1980.
6. **Clancy, A. N., A. G. Singer, F. Macrides, F. H. Bronson, and W. C. Agosta.** Experiential and endocrine dependence of gonadotropin responses in male mice to conspecific urine. *Biol. Reprod*. 38: 183–191, 1988.
7. **Clulow, F. V., and J. R. Clarke.** Pregnancy block in *Microtus agrestis*, an induced ovulator. *Nature* 218: 511, 1968.
8. **Clulow, F. V., and P. E. Langford.** Pregnancy block in the meadow vole, *Microtus pennsylvanicus*. *J. Reprod. Fertil*. 24: 275–277, 1971.
9. **Dluzen, D. E., V. D. Ramirez, C. S. Carter, and L. L. Getz.** Male vole urine changes luteinizing hormone-releasing hormone and norepinephrine in female olfactory bulb. *Science* 212: 573–575, 1981.
10. **Dominic, C. J.** The origin of pheromones causing pregnancy block in mice. *J. Reprod. Fertil*. 10: 469–472, 1965.
11. **Eichenbaum, H., A. Fagan, and N. J. Cohen.** Normal olfactory discrimination learning set and facilitation of reversal learning after medial-temporal damage in rats: implications for an account of preserved learning abilities in amnesia. *J. Neurosci*. 6: 1876–1884, 1986.
12. **Eichenbaum, H., and T. Otto.** The hippocampus—what does it do? *Behav. Neural Biol*. 57: 2–36, 1992.
13. **Eleftheriou, B. E., F. H. Bronson, and M. X. Zarrow.** Interaction of olfactory and other environmental stimuli on implantation in the deer mouse. *Science* 137: 764, 1962.
14. **Gavish, L., C. S. Carter, and L. L. Getz.** Male-male interactions in prairie voles. *Anim. Behav*. 31: 511–518, 1983.
15. **Getz, L. L., B. McGuire, J. Hofmann, T. Pizzuto, and B. Frase.** Social organizations and mating system of the prairie vole, *Microtus ochrogaster*. In: *Social Systems and Population Cycles in Voles*, edited by R. H. Tamarin, R. S. Ostfeld, S. R. Pugh, and G. Bujalska. Boston: Birkhauser, 1990, p. 69–79.
16. **Heske, E. J., and R. J. Nelson.** Pregnancy interruption in *Microtus ochrogaster*: laboratory artifact or field phenomenon. *Biol. Reprod*. 31: 97–103, 1984.
17. **Johnston, R. E.** Olfactory and vomeronasal mechanisms of communication. In: *Taste, Olfaction, and the Central Nervous System*, edited by P. W. Pfaff. New York: Rockefeller University Press, 1985.
18. **Kaba, H., and E. B. Keverne.** The effect of microinfusions of drugs into the accessory olfactory bulb on the olfactory block to pregnancy. *Neuroscience* 25: 1007–1011, 1988.
19. **Kaba, H., A. E. Rosser, and E. B. Keverne.** Hormonal enhancement of neurogenesis and its relationship to the duration of olfactory memory. *Neuroscience* 24: 93–98, 1988.
20. **Kawate, M.** Pregnancy failure and suppression by female-female interactions in enclosed populations of the red-backed vole, *Clethrionomys rufocanus bedfordiae*. *Behav. Ecol. Sociobiol*. 20: 89–97, 1987.
21. **Kesner, R., P., and J. M. Williams.** Memory for magnitude of reinforcement: dissociation between the amygdala and hippocampus. *Neurobiol. Learn. Mem*. 64: 237–244, 1995.

22. **Keverne, E. B.** Pheromonal influences on the endocrine regulation of reproduction. *Trends Neurosci*. 6: 381–384, 1983.
23. **Keverne, E. B., and C. de la Riva.** Pheromones in mice: reciprocal interaction between nose and brain. *Nature* 296: 148–152, 1982.
24. **Kirkpatrick, B., C. S. Carter, S. W. Newman, and T. R. Insel.** Axon-sparing lesions of the medial nucleus of the amygdala decrease affiliative behaviors in the prairie vole (*Microtus ochrogaster*): behavioral and anatomical specificity. *Behav. Neurosci*. 108: 501–513, 1994.
25. **Kling, A.** Effects of amygdalectomy on social-affective behavior in nonhuman primates. In: *The Neurobiology of the Amygdala*, edited by B. E. Eleftheriou. New York: Plenum, 1972.
26. **Lloyd-Thomas, A., and E. B. Keverne.** Role of the brain and accessory olfactory system in the block to pregnancy in mice. *Neuroscience* 7: 907–913, 1982.
27. **Mallory, F. F., and R. J. Brooks.** Infanticide and pregnancy failure: reproductive strategies in the female collared lemming, *Dicrostonyx groenlandicus*. *Biol. Reprod*. 22: 192–196, 1980.
28. **Marchlewska-Koj, A., and J. Drozdowska.** Testosterone control of the pregnancy block pheromone in mice. *Folia Biol. (Praha)* 32: 301–306, 1984.
29. **Moffatt, C.** *Seasonal and Social Regulation of Reproductive Behavior in Female Prairie Voles (Microtus ochrogaster)* (PhD thesis). Baltimore, MD: Johns Hopkins University, 1994.
30. **Nelson, R. J., L. L. Badura, and B. D. Goldman.** Mechanisms of seasonal cycles of behavior. *Annu. Rev. Psychol*. 41: 81–108, 1990.
31. **Otto, T., F. Schottler, U. Staubli, H. Eichenbaum, and G. Lynch.** Hippocampus and olfactory discrimination learning: effects of entorhinal cortex lesions on olfactory learning and memory in a successive-cue, go-no-go task. *Behav. Neurosci*. 105: 111–119, 1991.
32. **Parkes, A. S., and H. M. Bruce.** Olfactory stimuli in mammalian reproduction. *Science* 134: 1049–1054, 1961.
33. **Paxinos, G., and C. Watson.** *The Rat Brain in Stereotaxic Coordinates* (3rd ed.). New York: Academic, 1997.
34. **Rajendren, G., and C. J. Dominic.** The male-induced pregnancy block (the Bruce effect) in mice: re-evaluation of the ability of exogenous progesterone in preventing implantation failure. *Exp. Clin. Endocrinol*. 89: 197–217, 1987.
35. **Richmond, M. E., and R. A. Stehn.** Microtine olfaction and reproductive behavior. In: *Mammalian Olfaction, Reproductive Processes, and Behavior*, edited by R. L. Doty. New York: Academic, 1976, p. 197–217.
36. **Scalia, F., and S. S. Winans.** The differential projections of the olfactory bulb and accessory olfactory bulb in mammals. *J. Comp. Neurol*. 161: 31–55, 1975.
37. **Scalia, F., and S. S. Winans.** New perspectives on the morphology of the olfactory system: olfactory and vomeronasal pathways in mammals. In: *Mammalian Olfaction, Reproductive Processes, and Behavior*, edited by R. L. Doty. New York: Academic, 1976, p. 7–28.
38. **Selway, R., and E. B. Keverne.** Hippocampal lesions are without effect on olfactory memory formation in the context of pregnancy block. *Physiol. Behav*. 47: 249–252, 1990.
39. **Singer, A. G., A. N. Clancy, F. Macrides, W. C. Agosta, and F. H. Bronson.** Chemical properties of a female mouse pheromone that stimulates gonadotropin secretion in males. *Biol. Reprod*. 38: 193–199, 1988.
40. **Staubli, U., G. Ivy, and G. Lynch.** Hippocampal denervation causes rapid forgetting of olfactory information in rats. *Proc. Natl. Acad. Sci. USA* 81: 5885, 1984.
41. **Sullivan, R. M., and D. A. Wilson.** Role of the amygdala complex in early olfactory associative learning. *Behav. Neurosci*. 107: 254, 1993.
42. **Van der Lee, S., and L. M. Boot.** Spontaneous pseudopregnancy in mice. *Acta Physiol. Pharmacol. Neerlandica* 4: 442–443, 1955.
43. **Whitten, W. K.** Modification of the oestrus cycle of the mouse by external stimuli associated with the male. *J. Endocrinol*. 13: 399–404, 1956.
44. **Witt, D. M., C. S. Carter, K. Carlstead, and L. Read.** Sexual and social interactions preceeding and during male-induced oestrus in prairie voles, *Microtus ochrogaster*. *Anim. Behav*. 36: 1465–1471, 1988.
45. **Wysocki, C. J., J. L. Wellington, and G. K. Beauchamp.** Access of urinary nonvolatiles to the mammalian vomeronasal organ. *Science* 207: 781–783, 1980.