1990

Intracerebral Injections of Morphiceptin into the Medial Preoptic Area Produce a Delay in the Initiation of Male Rat Sexual Behavior

Leslie Matuszewich '90
Illinois Wesleyan University

Recommended Citation

INTRACEREBRAL INJECTIONS OF MORPHICEPTIN INTO THE MEDIAL PREOPTIC AREA PRODUCE A DELAY IN THE INITIATION OF MALE RAT SEXUAL BEHAVIOR.

BY

LESLIE MATUSZEWICH

Department of Psychology
Illinois Wesleyan University
May 1990

ACKNOWLEDGEMENTS

I would like to thank Dr. Dornan for showing me "the light" and straightening out my life before I forfeited accomplishing anything of importance and went off to have babies. I will let the rats make the babies for a couple years.

Also I would like to thank the entire lab group--Chris Ballack, Kellie Jones, Peter Malen and Melissa Peterson--for making life easier at times and definitely more interesting.

To my review committee and especially Dr. Clavadetscher for additional emotional and financial support on behalf of the psychology department.

I would like to thank my family and my roommate, Jennifer Ahearn, who patiently learned more about the sexual practices of rats in the last year than they ever wanted to know.

Finally and most importantly, I would like to thank Carlo D'Agostino who understands how much this project has meant to me and whose patience and understanding has endured unwavering. I hope that it is your patience that I continue to try for many years to come.

ABSTRACT

Behavioral experiments examined the role of morphiceptin in male rat copulatory behavior. Male copulatory behavior was recorded subsequent to bilateral injections of either 10, 500, or 1000 ng of morphiceptin into the medial preoptic area (MPOA) in sexually vigorous male rats. In the first experiment, all three doses of morphiceptin injected bilaterally into the MPOA produced a dramatic delay in the initiation of copulation. Both mount and intromission latencies significantly increased following injections of all three doses of morphiceptin when compared to saline injected controls. No other parameter was effected. In experiment 2, the inhibitory effects of morphiceptin on male copulatory behavior were abolished by pretreatment with naloxone 20 minutes prior to intracerebral morphiceptin injections. This study represents an attempt at a pharmacological characterization of the inhibitory effects of opioids on male rat sexual behavior. The results of experiment 1 indicate that mu receptors located within the MPOA mediate the initiation of male rat copulatory behavior.

GENERAL INTRODUCTION

A richly interconnected, sexually dimorphic circuit which includes the medial amygdala (MA), the bed nucleus of the stria terminalis (BnST), and the medial preoptic area (MPOA) has been reported to be an important pathway for the expression of male sexual behavior in rodents (see (9) for review). In particular, lesions of the MPOA have been reported to severely impair copulation and even to eliminate sexual behavior completely in a wide range of species (1,4,12,29,35); while electrical stimulation of the MPOA enhances the expression of male copulatory behavior (17,19). The dramatic effects on male copulatory behavior following lesions or electrical stimulation of the MPOA as compared to other brain structures, imply that the MPOA plays a central role in regulating male sexual behavior in the laboratory rat (see (31) for review).

Although the importance of this interconnected circuit for male rat sexual behavior has been clearly demonstrated, one of the fundamental questions that remains to be answered is the identity of the neurotransmitter(s) within the circuit that regulates male copulatory behavior. Recently, experimental interest has focused on the idea that neuropeptides within the sexually dimorphic circuit play an important role in the regulation of male sexual behavior (7,8,33,34), (see (9) for review). One class of neuropeptide which is found in this circuit is the opioid peptide. Indeed, there is a wealth of information which reveals that the administration of opioid agonists inhibits sexual behavior in mammals, non-human primates and humans (13,18,32), see (27) for review.

One opioid of particular interest is beta-endorphin. Meyerson and Terenius

reported that three different doses (1, 3 and 30 micrograms) of beta-endorphin injected into the lateral ventricles (ICV) produced a dose-dependent inhibition of copulatory behavior in male rats. This effect was blocked by peripheral injections of naltrexone 30 minutes before ICV injections of beta-endorphin (21). In a subsequent study, Meyerson again reported an inhibition of copulatory behavior following injections of beta-endorphin at lower doses (0.5 and 1.0 micrograms) into the cerebral ventricles. Interestingly, he also reported that although morphine, another opioid, had similar effects on copulatory behavior as beta-endorphin, morphine was not specific in that it suppressed a number of behaviors that beta-endorphin did not (20).

It is surprising that until 1987 no published reports existed in the literature on the effects of opioid agonists on male sexual behavior following injections directly into brain loci implicated in male sexual behavior. Hughes et al. (14) were the first to examine the effects of injections of beta-endorphin into the sexually dimorphic circuit. Bilateral injections of beta-endorphin into the MPOA in male rats produced a dose-dependent inhibition of male copulatory behavior: mount, intromission and ejaculation latencies increased while the mount rates (mounts/min) decreased. In order to assess the anatomical specificity of action of beta-endorphin on male sexual behavior, in that same study beta-endorphin was also injected into the Bnst, another area implicated in male sexual behavior and located near the MPOA. Identical doses of beta-endorphin which produced a profound inhibition of male copulatory behavior in the MPOA, had no effect following bilateral injections into the BnST (14).

Recently, there has been much speculation in the literature about the possible involvement of different opioid receptors in the regulation of male copulatory behavior.

The impetus for this has been derived from studies which have reported that selective activation of different opioid receptors have differential effects on sexual receptivity in ovariectomized-estrogen primed female rats. It appears that activation of high affinity mu receptors inhibit sexual receptivity, whereas mu_2 or delta receptor activation produce an inhibition (26,28). Based on such findings on female sexual behavior, studies have expanded to examine the behavioral effects of differential opioid receptor activation on copulatory behavior in male rats. Indeed, although opioid agonists have long been recognized as playing a predominantly inhibitory role in male sexual behavior, this dogma has recently been challenged. Band and Hull reported that unilateral injections of low doses of morphine (a relatively selective mu agonist) and dynorphin (a kappa agonist) into the MPOA of male rats produced a facilitation in copulatory behavior at 10-100 pmol. Males injected with a higher dose of morphine (6 nmol), however, showed an inhibition in copulatory behavior by failing to intromit after the second ejaculation. Band and Hull postulated that the different effects of morphine on male sexual behavior could be attributed to multiple receptor subtype activation (2). Indeed, morphine is only 50 times more potent at mu receptors that at delta receptors (23). Given the relative lack of specificity of morphine for individual opioid receptor subtypes, it is possible that the differential effects of morphine could be attributed to activation of different opioid receptor subtypes.

Therefore, a crucial step in assessing the role of opioids on male copulatory behavior is to elucidate the receptor subtype involved. Presently, however, it is not clear which receptor type mediates the inhibition of male copulatory behavior following central administration of opioid agonist. For example, beta-endorphin displays equal affinity to

mu and delta receptors (16). Consequently, it is impossible to assess based on the results of the Hughes et al study which opioid receptor type located within the MPOA mediates the inhibition of male copulatory behavior. In contrast, morphiceptin is considered a selective opioid receptor agonist with a 1000 times greater affinity for mu than delta or kappa receptors (5,6). Therefore, in the present study, I assessed the role of mu receptors in male copulatory behavior following bilateral injections of morphiceptin into the MPOA.

GENERAL METHODS

Animals and Surgery:

Thirty adult male Long-Evan rats purchased from Charles River, Wilmington, MA, were used. The animals weighed between 375 and 450 grams. The rats were housed individually and maintained in a controlled environment on a light/dark cycle (lights on at 6:00 and off at 21:00). Animals were handled on a regular basis to minimize stress during intercerebral injections. Food and water were available ad lib throughout the experiment. Stimulus females of the same strain were ovariectomized under ether. Fifty-three hours and 4 hours before each behavioral test, females were injected subcutaneously with 10 micrograms of estradiol benzoate and 1 microgram progesterone respectively, to ensure maximal sexual receptivity. Each male was given preoperative screening tests in which it was placed with a fully receptive female until one ejaculation was achieved. Only males that had ejaculated at least twice during the screening tests were subsequently used. Following the second or third successful preoperative test session, each male was anesthetized with Somnotol (50mg/kg) and received a pair of stereotaxically implanted 22-gauge stainless steel guide cannulae, aimed 2mm above the medial preoptic area (MPOA) (from bregma, AP = +2/2; ML = -0.5; and DV = -6.3) using the atlas of Paxinos and Watson as a guide (24). The cannulae were secured with cranioplastic cement.

Behavioral Testing:

One week following the surgery the males were given a postoperative test in rectangular test arenas (20 x 15 x 14 in.) with standard bedding to obtain baseline measures. Ovariectomized, steroid-primed female rats were placed in the arena with the male rat. If a male failed to mount or intromit within the first five minutes of the baseline test, he was given another baseline test one week later. Those that failed the second baseline test were excluded from this study.

All males that successfully completed a baseline test received injections of saline or morphiceptin seven days later. During experimental and baseline tests several measures were taken: mount latency (ML), the interval from the introduction of the female to the first mount by the male; intromission latency (IL), the interval from the introduction to the first intromission; the ejaculation latency (EL), the interval from the first intromission to the first ejaculation; the post-ejaculatory interval (PEI), the interval from the first ejaculation to the next mount; the mount frequency (MF), the number of mounts without intromission between the introduction and the ejaculation; the intromission frequency (IF), the number of intromissions between the introduction and the ejaculation; and the number of crawls exhibited. The last measure was taken to provide another measure of sexual motivation beside mount latency. The test period lasted either 30 minutes or until the first mount following ejaculation (PEI). The intercopulatory interval (ICI), mean interval between intromissions, was also obtained by dividing the overall ejaculation latency by the intromission frequency. Animals that failed to mount, intromit or ejaculate during the morphiceptin testing were assigned latencies of 900 second, the duration of the

observation period (14).

Intracerebral Injections:

Rats were taken from their cages and individually placed on a table in a low light, low noise situation. The 26 gauge inner cannula (extending 2 mm past the guide) was attached to a 2 microliter syringe by a plastic tube. Distilled water was drawn through the tube until 1 microgram of distilled water could be drawn and expelled. An air bubble was then drawn through the tube to mark the separation between the distilled solution and the morphiceptin solution. Half a microliter of either 10, 500 or 1000 nanogram of morphiceptin in a 9% saline solution or saline was injected manually over 60 seconds into each side of the brain. The inner cannula was left in place for 60 seconds following the injection to insure that the solution diffused downward rather than returning up the cannula. If a discrepancy arose as to the movement of the air bubble, another dose was administered. Five minutes after the injection, the testing session began.

Histological Analysis:

Following data acquisition, all animals were anesthetized with an overdose of Somnotol. Brains were removed and 46 micron sections taken using a cryostat. Sections were stained using cresyl violet and the location of each cannula placement was verified.

Data Analysis:

Unless otherwise stated, all data were analyzed using an unweighted means-analysis of variance (ANOVA) in a repeated measures split-plot design. Post-hoc

comparisons of treatment means were assessed using a modified Tukey's ratio, required when an unweighted-means of analysis is employed (15).

EXPERIMENT 1: PREOPTIC INJECTIONS OF MORPHICEPTIN INHIBIT MALE COPULATORY BEHAVIOR

Method:

Thirty-one adult male Long Evans rats (375-450 grams) were divided into four groups. Three groups received bilateral injections of either 10, 500, or 1000 ng of morphiceptin/cannula in a volume of 0.5 microliter per cannula (Sigma Chemical Company, lot No. 84F-58352) dissolved in 0.9% saline into the MPOA. The fourth group was injected with saline.

Results:

Of the thirty-one animals that began the study, two had both cannulae located outside the MPOA, four had only one cannulae located within the MPOA, and three never satisfied criterion at the postoperative baseline test. That left twenty-two animals for the data analysis (controls, n = 7; 10 ng, n = 3; 500 ng, n = 6; 1000 ng, n = 7, (see figure 1 for a representative placement site). As illustrated in Table 1 bilateral injections of three different doses of morphiceptin significantly delayed the initiation of copulatory behavior compared to an injection of saline alone. This was revealed by a significant main effect on mount and intromission latencies $F_{(3,18)} = 6.68$, $p < 0.01$); $F_{(3,18)} = 4.57$, $p < 0.01$, respectively). This is also illustrated in figures 2 and 3. Post hoc analysis, however, ·

revealed that morphiceptin did not increase mount and intromission latencies in a dose-dependent manner. No other parameter was affected. For example, as can be seen in figure 4, morphiceptin failed to significantly alter ejaculation latencies ($F = 1.26$, $p > 0.05$). As illustrated in table 1, following injections of morphiceptin, 14 % (1000 ng) and 28 % (500 ng) of the males failed to mount or intromit.

Bilateral injections of morphiceptin into the MPOA failed to alter significantly ejaculation latency ($F = 1.26$, $p > 0.05$), the PEI ($F = 0.47$, $p > 0.05$) or the mount and intromission frequencies ($F = 1.90$, $p > 0.05$; $F = 0.23$, $p > 0.05$, respectively) when compared to the saline injections (see Figure 4, and Table 1).

EXPERIMENT 2: PRETREATMENT WITH NALOXONE BLOCKED THE EFFECTS OF MORPHICEPTIN INJECTIONS ON COPULATORY BEHAVIOR

The preceding experiment demonstrated that bilateral injections of morphiceptin into the MPOA produced a dramatic inhibition of male copulatory behavior when compared to saline injected controls. In this experiment, we examined whether the inhibitory effects of morphiceptin on male copulatory could be blocked with pretreatment of a non-selective opioid antagonist (naloxone).

Method:

Following completion of the last behavioral test in experiment 1, all remaining animals were randomly divided into two groups. Group 1 received an IP injection of 1mg/kg naloxone (lot No. 128F-0264) 20 minutes prior to bilateral injections of 1000 ng of morphiceptin directly into the MPOA. Group 2 was pretreated with saline. Since the

1000 ng dose of morphiceptin produced the greatest delay in the initiation of copulation, we decided to examine the effects on male copulatory behavior following pretreatment with naloxone using bilateral injections of 1000 ng of morphiceptin into the MPOA.

Results:

As in Experiment 1, bilateral injections of morphiceptin increased mount and intromission latencies in saline pretreated animals. Pretreatment with naloxone completely abolished the inhibitory effects of morphiceptin (see figure 5).

DISCUSSION

Bilateral microinjections of three different doses of morphiceptin in the MPOA produced a dramatic delay in the initiation of copulation in sexually vigorous male rats when compared to saline injected controls. This inhibition was completely abolished by pretreatment 20 minutes prior to morphiceptin microinjections with naloxone (1mg/kg) injected IP. These results provide further support that the MPOA is an important site of action for the inhibitory effects of peripherally administered opioids. Moreover, these results strongly suggest that the delay in the initiation of copulation that is commonly observed following peripheral or central injections of opioids is mediated by mu receptors located within the MPOA.

The results of this study partly conflict with other studies which have assessed male copulatory behavior following administration of non-selective opioid agonists. For example, no effect was observed on ejaculatory threshold following injections of morphiceptin (see table 1). This discrepancy can be partly explained by the pharmacological profile of the agonists employed in the various studies. For example, in the Hughes et al. study, significant increases in mount, intromission and ejaculation latencies were observed following bilateral injections of beta-endorphin into the MPOA (14). Beta-endorphin, a prototypical opioid, binds equally well to both mu and delta receptors. Thus, the inhibition on male sexual behavior observed in the Hughes et al. study may have been partially mediated via delta receptors. Indeed, pretreatment with a putative delta receptor antagonist (ICI 174864) prevented the inhibition of male sexual

behavior following bilateral injections of beta-endorphin into the MPOA. Therefore, the results from my study taken together with Hughes' study, suggest that mu receptors mediate the initiation, while delta receptors may be involved in the ejaculatory threshold or the resolution of the copulatory sequence once copulation is initiated.

In the literature it has been frequently reported that beta-endorphin injections produce a "MPOA lesion-like behavior" in male rats; that is, the male vigorously pursues the female but his performance halts at the point when he would normally mount her (14,20,21). This is not surprising based on the findings of several recent studies which have reported that neurochemical lesions of the MPOA in male rats lead to a dramatic disruption of male copulatory behavior but have no effect on operant responding for a sexual receptive female (10). In this type of paradigm males will bar press reliably for a female, but once the female is introduced, the males fail to mount or intromit. MPOA lesion-like behavior was repeatedly seen in this study as well. Following injections of all three doses of morphiceptin into the MPOA the males would almost immediately pursue and investigate the female anogenitally. Indeed contact latencies remained relatively low (means in seconds: 1000 ng = 72.0; 500 ng = 410.81; 10 ng = 18.66) following morphiceptin injections despite the dramatic increase in mount and intromission latencies. Therefore, it seems that morphiceptin like beta-endorphin injections into the MPOA does not interfere with the initial interest or access to the female, but interferes with an organization component of the motor pattern of sexual behavior.   Beach (3) proposed that, contrary to viewing sexual behavior as a unitary construct, two separate mechanisms were involved in male reproductive behavior: a sexual arousal mechanism and a copulatory mechanism. He suggested that the arousal mechanism mediates the male's

initiation of the copulatory sequence, as well as the resumption of copulation following ejaculation. The copulatory mechanism was assumed to maintain copulatory behavior by summating the excitation of each successive intromission until ejaculation occurred. Since its original formulation the "two factor" theory of Beach has received considerable attention. As a result, its conceptual framework has been continually revised. Based on a factor analysis of normative data on sexual behavior in male rats, Sachs (30) subsequently subdivided the copulatory mechanism into further dimensions, one of which he referred to as a "copulatory rat factor". This factor contained three components: inter-intromission interval (which has been referred to as the ICI), ejaculation latency, and the post-ejaculatory interval (PEI). The reason for the inclusion of the PEI in the theoretical copulatory mechanism framework was to account for the relative independence of the PEI from mount and intromission latencies (two behavioral components associated with arousal). Collectively, the results of this study strongly suggest that in addition to the mediation of the initiation of copulation, mu receptors located within the MPOA may be partly involved in arousal but have no role in the copulatory mechanism of male rat sexual behavior.

For example, as previously mentioned following the termination of a pursuit, the male would show considerable interest in the female but would not mount her. This was often followed by flank grooming and scratching. On other occasions, however, after an abortive mount, the male would lose interest in the female, sometimes for as long as 2 or 3 minutes.

In this study motor activity was not measured. The rationale for this is straight forward, there are many studies which have now been published using a variety of *

approaches to measure motor activity following the administration of opioid agonists, which have concluded that at low doses, opioids inhibit male copulatory behavior without affecting locomotor activity (11,14,21,22,25). The findings of low contact latencies following morphiceptin injections further substantiate this conclusion that the disruption of male sexual behavior was not due to a general behavioral inhibition.

In conclusion, the results of this study further support the importance of the opioid innervation of the MPOA in the regulation of male copulatory behavior. Furthermore, as a result of the pharmacological characterization of the specific receptor involved in the inhibition of male copulatory behavior, these results suggest that the initiation of copulation in the male rat is mediated via mu receptors and the ejaculatory threshold via another opioid receptor. Clearly, further research remains to be done using selective mu antagonists, as well as highly selective agonists before the role of different opioid receptors in the regulation of male copulatory behavior is clearly elucidated. Nonetheless, it is hoped that these results will facilitate the understanding of the role of different opioid receptor regulation of male rat copulatory behavior and as a result provide further insight into the role of endogenous opioids in the neuroregulation of male sexual behavior.

REFERENCES

1. Arendash, G.W. and Gorski, R.A. Effects of Discrete Lesions of the Sexually Dimorphic Nucleus of the Preoptic Area or Other Medial Preoptic Regions on the Sexual Behavior of Male Rats. Brain Research Bulletin,10:147-154, 1983.

2. Band, L.C. and Hull, E.M. Morphine and Dynorphin (1-13) microinjected into the medial preoptic area and nucleus accumbens: effects on sexual behavior in male rats. Submitted for Publication,1990.

3. Beach, F.A. Characteristics of masculine "sex drive". In: *Nebraska Symposium on Motivation*, edited by Jones, M.R. : University of Nebraska Press, 1956, p. 1-32.

4. Brackett, N.L., Iuvone, P.M. and Edwards, D.A. Midbrain lesions, dopamine and male sexual behavior. Behavioural Brain Research,20:231-240, 1986.

5. Chang, K.J., Cautrecasas, P., Wei, E.T. and Chang, J.K. Analgesic activity of intracerebroventricular administration of morphiceptin and beta-casomorphins: Correlation with morphine (mu) receptor binding affinity. Life Sciences,30:1547-1551, 1982.

6. Chang, K.J., Killian, A., Hazum, E., Cautrecasas, P. and Chang, J.K. Morphiceptin (NH2-Tyr-Pro-Phe-Pro-CONH2): A potent and specific agonist for morphine (mu) receptors. Science,212:75-77, 1981.

7. Clark, J.T., Kalra, S.P. and Kalra, P.S. Neuropeptide Y stimulates feeding but inhibits sexual behavior in rats. Endocrinology,117:2435-2442, 1985.

8. Dornan, W.A. and Malsbury, C.W. Peptidergic control of male rat sexual behavior: the effects of intracerebral injections of Substance P and cholecystokinin. Physiology and Behavior,46:547-556, 1989.

9. Dornan, W.A. and Malsbury, C.W. Neuropeptides and male sexual behavior. Neuroscience and Biobehavioral Reviews,13:1-15, 1989.

10. Everitt, B.J. and Stacey, P. Studies of instrumental sexual behavior in the male rat using second order schedules of reinforcement II: Effects of preoptic area lesions, castration, and testosterone. Journal of Comparative Psychology,101:407-419, 1987.

11. Gessa, G.L., Paglietti, E. and Pellegrini-Quarantotti, B. Induction of copulatory behavior in sexually inactive rats by naloxone. Science,204:203-205, 1979.

12. Ginton, A. and Merari, A. Long range effects of MPOA lesion on mating behavior in the male rat. Brain Research,120:158-163, 1977.

13. Greenberg, A. Effects of opiates on male orgasm. Medical Aspects of Human Sexuality,18:207-210, 1984.

14. Hughes, A.M., Everitt, B.J. and Herbert, J. Selective effects of B-endorphin infused into the hypothalamus, preoptic area and bed nucleus of the stria terminalis on the sexual and ingestive behavior of male rats. Neuroscience,23:1063-1073, 1987.

15. Kirk, Roger E. *Experimental Design: Procedures for the Behavioral Sciences*, Belmont:Brooks/Cole Publishing Company, 1969. Ed. 2 pp. 245-255.

16. Lee, N. and Smith, A. A protein-lipid model of the opiate receptor. Life Sciences,26:1459-1464, 1980.

17. Malsbury, C.W. Facilitation of male rat copulatory behavior by electrical stimulation of the medial preoptic area. Physiology and Behavior,7:797-805, 1971.

18. McIntosh, T.K., Vallano, M. and Barfield, R.J. Effects of morphine, B-endorphin and naloxone on catecholamine levels and sexual behavior in the male rat. Pharmacology Biochemistry & Behavior,13:435-441, 1979.

19. Merari, A. and Ginton, A. Characteristics of exaggerated sexual behavior induced by electrical stimulation of the medial preoptic area in male rats. Brain Research,86:97-108, 1975.

20. Meyerson, B.J. Comparison of the effect of B-endorphin and morphine on·exploratory ·

and socio-sexual behavior in the male rat. European Journal of Pharmacology,69:453-463, 1981.

21. Meyerson, B.J. and Terenius, L. B-Endorphins and Male Sexual Behavior. European Journal of Pharmacology,42:191-192, 1977.

22. Murphy, M.R. Methadone reduces sexual performance and sexual motivation in the male syrian golden hamster. Pharmacology Biochemistry & Behavior,14:561-567, 1981.

23. Paterson, S., Robson, L. and Kosterlitz, H. Classification of opioid receptors. British Medical Bulletin,39:31-36, 1983.

24. Paxinos, G. and Watson, C. *The rat brain in stereotaxic coordinates*, Sydney:Academic Press, 1982.

25. Pellegrini-Quarantotti, B., Corda, M.G., Paglietti, E., Biggio, G. and Gessa, G.L. Inhibition of copulatory behavior in male rats by D-ala2-Met-Enkephalinamide. Life Sciences,23:673-678, 1978.

26. Pfaus, J.G. and Gorzalka, B.B. Selective activation of opioid receptors differentially affects lordosis behavior in female rats. Peptides,8:309-317, 1987.

27. Pfaus, J.G. and Gorzalka, B.B. Opioids and sexual behavior. Neuroscience and ·

Biobehavioral Reviews,11:1-34, 1987.

28. Pfaus, J.G., Pendleton, N. and Gorzalka, B.B. Dual effects of morphiceptin on lordosis behavior: possible mediation by different opioid receptors subtypes. Pharmacology Biochemistry and Behavior,24:1461-1464, 1986.

29. Powers, J.B., Newman, S.W. and Bergondy, M.L. MPOA and BNST lesions in male Syrian hamsters: differential effects on copulatory and chemoinvestigatory behaviors. Behavioural Brain Research,23:181-195, 1987.

30. Sachs, B.D. Conceptual and neural mechanisms of masculine copulatory behavior. In: *Sex and Behavior: Status and Prospectus*, edited by McGill, T.E., Dewsbury, D.A. and Sachs, B.D. New York: Plenum Press, 1978, p. 267-296.

31. Sachs, B.D. and Meisel, R.L. The physiology of male sexual behavior. In: *The physiology of reproduction*, edited by Knobil, E., Neill, J. and et al. New York: Raven Press Ltd., 1988, p. 1393-1485.

32. Seevers, M. Opiate addiction in the monkey. I. Methods of studyt. Journal of Pharmacology and Experimental Therapeutics,56:147-156, 1936.

33. Sirinathsinghji, D.J.S. Inhibitory influence of corticotropin releasing factor on components of sexual behaviour in the male rat. Brain Research,407:185-190, 1987.

34. Stoneham, M.D., Everitt, B.J., Hansen, S., Lightman, S.L. and Todd, K. Oxytocin and sexual behaviour in the male rat and rabbit. Journal of Endocrinology,107:97-106, 1985.

35. Szechtman, H., Caggiula, A.R. and Wulkan, D. Preoptic knife cuts and sexual behavior in male rats. Brain Research,150:569-591, 1978.

TABLE 1
Experiment 1: Effects of Injections of Saline or Morphiceptin into the MPOA on Male Sexual Behavior

		Morphiceptin		
Measures	Saline	10 ng	500 ng	1000 ng
ML[a]				
Baseline	7.38 ± 1.36	11.80 ± 5.7	69.86 ± 2.6	15.67 ± 7.7
Experimental	9.96 ± 2.07	398.90 ± 231.1 †	67.75 ± 152.73 †	473.80 ± 104.6 †
MF				
Baseline	6.86 ± 1.55	2.33 ± 1.30	5.50 ± 0.88	6.67 ± 1.56
Experimental	8.86 ± 2.20	3.30 ± 1.45	5.00 ± 2.31	5.80 ± 0.98
IL				
Baseline	18.76 ± 10.08	12.40 ± 5.40	21.80 ± 10.94	50.38 ± 13.80
Experimental	59.43 ± 30.60	400.70 ± 229.60 †	521.88 ± 166.20 †	608.12 ± 96.70 †
IF				
Baseline	8.71 ± 1.98	5.00 ± 1.50	7.67 ± 2.22	5.67 ± 1.48
Experimental	7.57 ± 1.54	6.70 ± 2.72	5.33 ± 2.63	5.00 ± 1.80
EL				
Baseline	349.94 ± 92.5	168.77 ± 52.70	236.30 ± 46.60	189.90 ± 39.90
Experimental	338.30 ± 82.94	359.10 ± 10.90	543.30 ± 135.20	297.00 ± 126.70
ICI				
Baseline	43.51 ± 6.71	33.87 ± 3.33	27.36 ± 1.89	38.55 ± 12.71
Experimental	43.40 ± 4.58	80.31 ± 34.25	43.60 ± 8.93	31.69 ± 6.09
PEI				
Baseline	408.43 ± 28.33	392.70 ± 51.86	373.15 ± 17.25	355.40 ± 52.70
Experimental	361.60 ± 22.83	395.90 ± 73.60	227.50 ± 71.06	447.50 ± 90.27
% E				
Baseline				
Experimental	100	83.3	100	66.6

[a] All latencies are in seconds. See text for full details.

† $p < 0.01$

FIGURE 1. Summarizes a representative bilateral cannula placement in males which received injections of either 10, 500 or 1000 ng of morphiceptin into the MPOA in experiments 1 and 2. Abbreviations: ac, anterior commissure; cc, corpus callosum; CPu, caudate putamen; GP, globus pallidus; f, fornix; ic, internal capsule; 3V, third ventricle; MPOA, medial preoptic area; oc, optic chiasm.
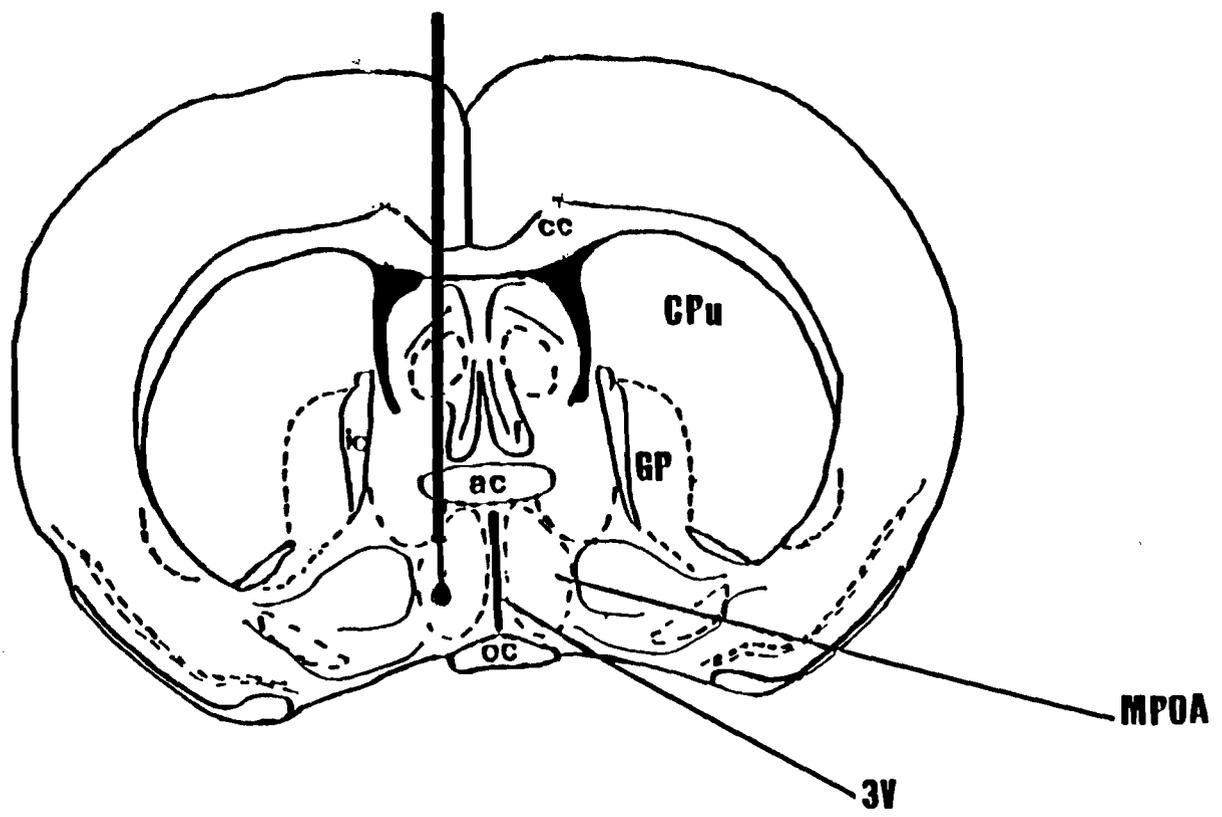
cc

CPu

GP

ac

oc

MPOA

3V

FIGURE 2. Comparison of the effect of morphiceptin injections to saline injections into the MPOA on mean mount latencies. The 10, 500 and 1000 ng doses delayed the occurrence of mounts significantly. Error bars in this and following figures display standard error on the difference between means.
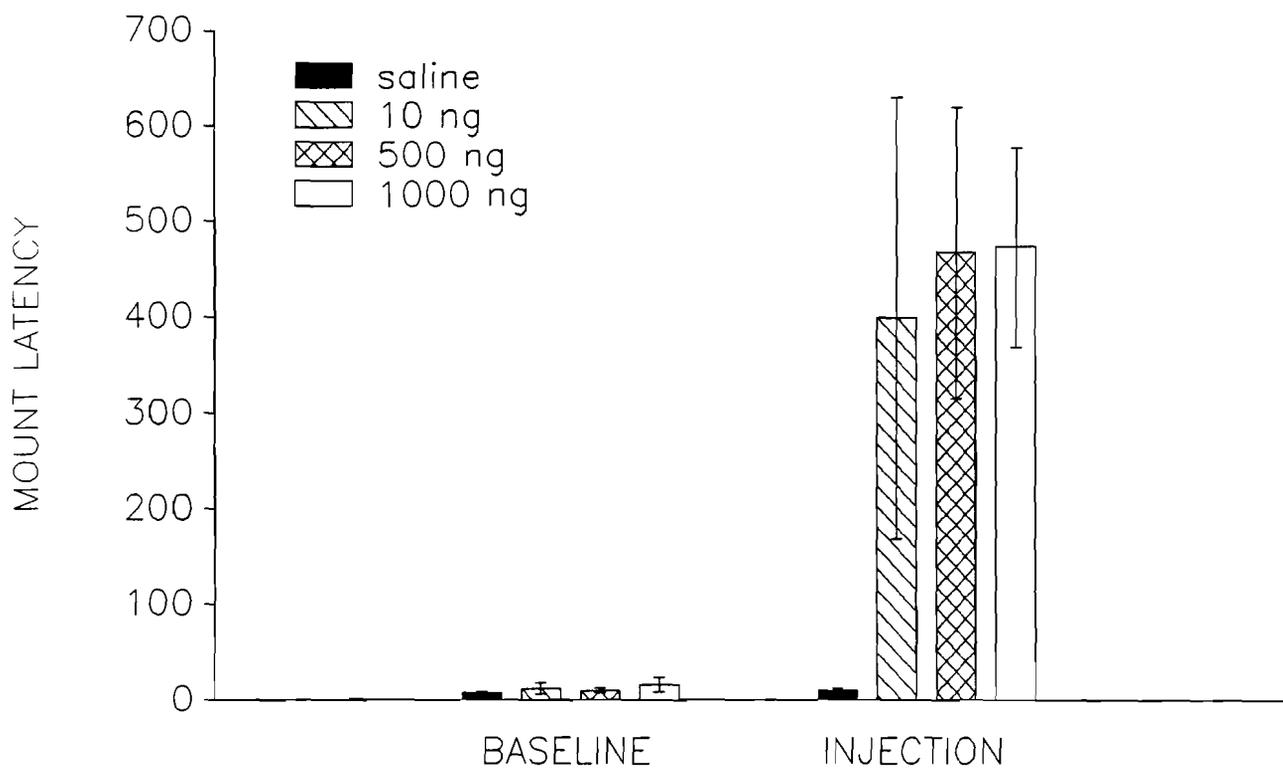
FIGURE 3. Comparison of the effect of morphiceptin injections to saline injections into the MPOA on mean intromission latencies. The 10, 500 and 1000 ng doses delayed the occurrence of intromissions significantly.

700

600

500

400

300

200

100

0

INTROMISSION LATENCY

■ saline
▨ 10 ng
▧ 500 ng
☐ 1000 ng

BASELINE

INJECTION

FIGURE 4. Comparison of the effect of morphiceptin injections to saline injections into the MPOA on mean duration to ejaculation from the first intromission. None of the three doses significantly effected the ejaculation latency.

FIGURE 5. Effects of naloxone + morphiceptin (1000 ng) injections compared to saline + morphiceptin (1000 ng) injections on mount, intromission and ejaculation latencies. Naloxone blocked the inhibitory effects of morphiceptin injections on mount and intromission latencies.