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ORIGINAL INVESTIGATION

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Effects of morphiceptin in the medial preoptic area on male sexual behavior

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Abstract Morphiceptin, a selective μ opioid agonist, injected into the medial preoptic area (MPOA), delayed the onset of copulation in male rats, but did not affect genital reflexes, sexual motivation or general motor activity. In a dose-dependent manner, morphiceptin (100 ng and 1000 ng) injected into the MPOA increased mount and intromission latencies. Similar injections of morphiceptin into the ventromedial hypothalamus had no effect on any parameter of copulation. The increase in copulatory latencies following the injection of the highest dose of morphiceptin was blocked by pretreatment with the opioid antagonist naloxone. In the X-maze task, morphiceptin had no effect on sexual motivation, as measured by the percentage of trials on which the male chose the female's chamber, but it increased the number of trials in which the subject did not select a chamber within 60 s and the latency to the female the first time he chose her chamber. Similar to the copulation task, the mount and intromission latencies were also increased in the X-maze, after the male reached the female. Morphiceptin in the MPOA had no effect on ex copula genital reflexes, tested in restrained supine males, or on motor activity, tested in a grid box. These results suggest that morphiceptin disrupts either the specific copulatory somatomotor pattern or a more general motivational component.

Key words Male sexual behavior · Opioid peptides · Motivation · Medial preoptic area · μ-Receptors

Introduction

Opioids administered systemically and intracranially have been reported to affect sexual behavior in a number of species, including humans, nonhuman primates, and rodents (reviewed in Pfaus and Gorzalka 1987). The literature provides a general consensus that systemic opioid agonists interrupt male sexual behavior (reviewed in Hetta 1977; Mumford and Kumar 1979; McIntosh et al. 1980; Bitran and Hull 1987), while opioid antagonists facilitate it (Hetta 1977; Myers and Baum 1979; McIntosh et al. 1980). However, this generalization is not supported by all studies. Morphine decreased the time to the second ejaculation, thus facilitating ejaculation; however, many subjects failed to copulate beyond their first ejaculation, indicating an impairment of copulation (Agmo and Paredes 1988). Naloxone, an opioid antagonist, has been shown to facilitate one measure of copulation by decreasing the time and the number of intromissions preceding ejaculation (Myers and Baum 1979), to inhibit another measure of copulation by decreasing the percentage of males achieving ejaculation in castrates (Lieblich et al. 1985), or to have no effect on copulation (Agmo and Paredes 1988).

The specific effects of intracranial opioids on sexual functioning appear to depend upon the opioid agonist tested, as well as its dose. Due to its importance in male sexual behavior, the medial preoptic area (MPOA) has been one brain site explored with microinjections of opioids. Morphine microinjected into the MPOA produced a biphasic effect, with the highest dose (6 nmol) inhibiting the continuation of copulation after the second ejaculation, and the lower doses (10–100 pmol) facilitating copulation by decreasing the number of intromissions preceding ejaculation and the intromission latency in the second ejaculatory series (i.e., shortening the first post-ejaculatory interval) (Band and Hull 1990). The kappa opioid receptor agonist, dynorphin(1–13), produced the same facilitating effects as the lower doses of morphine in the MPOA.

β-Endorphin, a μ and *d* opioid receptor agonist, microinjected into the MPOA, produced a dose-dependent impairment of copulation, with increased mount, intromission and ejaculation latencies and a decrease in the percent of males copulating (Hughes et al. 1987; Van

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Furth et al. 1995). The more selective *d* opioid receptor agonist, met-enkephalin, increased ejaculation latency and the number of intromissions in an ejaculatory series (Van Furth et al. 1995). On the other hand, morphiceptin, a selective μ agonist (Chang et al. 1981), microinjected into the MPOA, resulted in a delay of copulatory behavior, specifically increasing mount and intromission latencies (Matuszewich and Dornan 1992). It has been proposed that μ receptors in the MPOA may contribute specifically to the regulation of the onset of copulation in the male rat (Matuszewich and Dornan 1992), whereas the *d* receptors may contribute to the continuation of the copulatory series (Van Furth et al. 1995). Thus, even within one brain site, different opioid receptor agonists affected different aspects of male rat copulatory behavior.

The initiation of copulation in the male rat involves several behavioral components – appetitive behavior, somatomotor patterns and genital reflexes. All of these components must be coordinated for the male to achieve successful intromission. The present experiments were conducted to test each of the components separately, in an attempt to explain the delay in copulation following a microinjection of morphiceptin into the MPOA.

Materials and methods

Subjects

Male Long-Evans/Blue Spruce rats (300–350 g), purchased from Harlan Sprague Dawley, were used in all experiments. They were individually housed in a controlled environment with food and water available ad libitum. Their light cycle was reversed, with lights off at 1100 hours and on at 2100 hours. Female Long-Evans rats were ovariectomized under ketamine hydrochloride (50 mg/kg) and xylazine hydrochloride (4 mg/kg) anesthesia. Estrus was induced in the females with an injection of 20 μg estradiol benzoate, 48 h prior to testing. "Principles of laboratory animal care" (NIH publication No. 85–23, revised 1985) were followed for all experiments.

Surgery and eannulae

Male subjects were anesthetized with ketamine hydrochloride (50 mg/kg) and xylazine hydrochloride (4 mg/kg) intramuscularly and placed into a Kopf stereotaxic frame. All rats in experiment 1a received bilateral 23 gauge thin wall cannulae (Small Parts), with the left caunula euding 1 mm above the MPOA (AP: 2.4 mm from bregma; ML: 0.2 mm; DV: –7.4 mm) and the right eannula euding 1 mm above the ventromedial hypothalamus (VMH) (AP: 0.2 mm from bregma; ML: 1.1 mm; DV: –8.2 mm).

In a pilot study, the effects on copulation of unilateral MPOA injections of 1000 ng morphiceptin were eompared with those of bilateral injections of 500 ng eaeh, using the coordinates of Matuszewich and Dornan (1992) (AP: 2.4 mm from bregma; ML: ±0.5 mm; DV: –7.4 mm). There was no statistical difference in the behavioral effects between bilateral and unilateral drug injections, so unilateral injections were used for all other studies.

Subjects nsed in experiments 1b, 2, 3 or 4 received unilateral 23 gauge eannulae aimed 1 mm above the MPOA (AP: 2.4 mm; ML: 0.2 mm; DV: –7.4 mm). Further details of the surgical procedure are reported in Warner et al. (1991). A stylet, the same length as the cannula, was inserted into each cannula to prevent the entry of foreign material when the animal was not being injected. In experiment 3, the male rats also reeeived an excision of their suspensory ligament to facilitate the continuous exposure of the glans penis from the penile sheath for genital reflex tests.

Drugs

Morphiceptin hydrochloride (Sigma Chemical) was dissolved in 1 μl cold saline immediately prior to microinjection. In experiment 1a, the subjects received unilateral microinjections of 0, 100 or 1000 ng morphiceptin (weight of the salt) into either the MPOA or the VMH, in a counterbalanced fashion. These doses were in the middle of the effective dose range used in a previons experimcnt (Matuszewich and Dornan 1992). In experiment 1b, an IP injection of either sterile water or 1 mg/kg naloxone hydrochloride (Sigma Chemical) was given 20 min prior to a microinjection of 1000 ng morphiceptin. In experiments 2 and 4, animals received 0 or 1000 ng morphiceptin in the MPOA. In experiment 3, microinjections of 0, 100, and 1000 ng morphiceptin were given. For delivery of microinjections, the inner stylet was removed and replaced with the injection needle, which was in turn connected via a 1-m length of polyethylene tubing to a 1 cc syringe filled with drug or vehicle. Microinjections were delivered over a 60-s period, with the needle remaining in place for an additional 30 s. After replacement of the stylet, the male was carried in his home cage to an adjacent testing room, where testing began 5 min after the injection.

Experimental design

Experiment 1a compared the effects on copulation of MPOA versus VMH microinjections of morphiceptin (0, 100, or 1000 ng). Experiment 1b tested whether a systemic injection of the opioid antagonist naloxone could block the effects of morphiceptin in the MPOA. Experiment 2 tested whether the delay in copulation observed with 1000 ng morphiceptin in the MPOA was due to deficits in sexual motivation or locomotor activity. Animals were tested in an X-maze, with a receptive female in one goal box, a male in the opposite box, and the other two goal boxes empty. On half the trials, the male was placed into the female's goal box and allowed one intromission before receiving a microinjection of drug or sterile saline vehicle. Sexual motivation was measured as the percentage of trials on which the male chose the female's goal box, out of the total number of trials on which he chose any goal box. Motor activity was assessed as the latency to reach goal boxes and the number of trials on which he failed to make a choice. Experiment 3 tested whether the morphiceptin induced delay resulted from inhibition of genital reflexes. The same doses as in experiment 1a were injected into the MPOA in counterbalanced order. Experiment 4 tested whether the highest dose of morphiceptiu affected locomotion in an open field apparatus. Motor activity was measured as the number of grid lines crossed and the number of rears.

Copulation tests

Mating tests were conducted during the dark period of the light-dark cycle, under dim red light, with an ovariectomized female rat in estrus. Each subject received three 30-min preoperative tests in his home cage. One week following surgery, each subject was given a postoperative behavioral test with a receptive female. Only those rats that copulated (aehieved at least one intromission) dnring the postoperative test were used in the experiment. In experiment 1a, each of the 16 rats was subsequently tested weekly, following microinjections of 0, 100, or 1000 ng morphieeptin into either the MPOA or the VMH, in a counterbalanced fashion. For experiment 1b, six males received a systemic injection of either vehicle or 1 mg/kg naloxone 20 min prior to an MPOA infusion of 1000 ng morphiceptin. The subsequent week, each subject received the opposite pretreatment. Each test lasted 30 min following the first intromission, or for a total of 30 min if no intromission occurred. The following measures were recorded during each test: mount and intromission latencies (time interval from the introduction of the female to the first mount or intromission); ejaculation latency (time from first intromission to first ejaculation); mount, intromission and ejaculation frequencies; post-ejaculatory interval (time from ejaculation to the subsequent intromission); interintromission interval (ejaculation latency divided by number of

intromissions preceding ejaculation); and intromission ratio [100×intromissions/(mounts+intromissions)].

X-maze tests

All maze tests were conducted in a plywood X-maze with four arms, each ending in a goal box. The subject was placed into the center hub of the maze and had 1 min to traverse the length of an arm (30 cm) and reach a goal box (30 cm×30 cm). The goal box was recessed from the arm and separated from the runway by a Plexiglas door, which was raised to allow the male to enter the goal box when he crossed a strip of black electrical tape at the end of the runway. A receptive female was in one goal box, a male was in the opposite goal box, and the remaining two boxes were empty. If the subject chose the female's goal box, he was permitted one intromission or 5 min without an intromission, and then was placed into the center of the maze again. If he chose any other box (empty or male's box), he remained in the chosen box for 30 s. A training or testing session ended when the male ejaculated, when he failed to move from the start area within 60 s on 30 trials, or if he chose the female's goal box but failed to intromit on three trials (15 min total). Each subject received maze training prior to surgery until he chose the female's goal box on at least 70% of the trials in one training session. After reaching this criterion, the animal received a unilateral cannula surgically implanted as described above.

One week following surgery, each of the 12 subjects received postoperative maze training until each again chose the female's goal box on 70% or more of the trials. One week after reaching criterion, either 0 or 1000 ng morphiceptin was microinjected through the cannula and the rat was then tested in the X-maze. The following measures were recorded: number of trials on which the male chose each goal box; latency from the start of each trial until he reached a goal box; the number of trials in which he failed to reach any goal box within 60 s; latencies to the first mount and first intromission; and the number of mounts and intromissions preceding ejaculation. On some test days, the subject received an intromission in the female's goal box prior to the microinjection of the drug. On other test days, no preinjection intromission occurred; the microinjection occurred first and then the subject was placed directly into the center of the maze. These slightly different procedures were counterbalanced with the two drug doses, with each male receiving all four treatments (0 or 1000 ng morphiceptin, with or without the preinjection intromission).

Genital reflex tests

Subjects were restrained in a supine position in a metal cylinder (10 cm diameter) mounted on a piece of Plexiglas. The lower part of their body protruded from the cylinder and was restrained with Velcro straps. The penile sheath was retracted and held in position for better viewing of reflexes. Prior to surgery, the subjects were adapted to this procedure on four separate occasions for 20 min. Following unilateral MPOA cannula placements, each of the 14 subjects received a postoperative test in the restrainer without drug. Once testing began, 0, 100, or 1000 ng morphiceptin was microinjected through the cannula and the rat was then immediately placed into a restrainer. The occurrence and time of the following measures were recorded: anteroflexions of the penis; seminal emissions, a discharge of seminal fluid usually accompanied by several rapid, brief penile erections and rostral movements of the testes within the scrotal sac; and glans erections of three gradations: E1, engorgement of the base of the glans; E2, tumescence involving both base and tip of the glans; and E3, engorgement of the base and intense flaring of the tip of the glans. Each test lasted 15 min from the first reflex, or 20 min if no reflex occurred.

Locomotor tests

Six of the animals used in experiment 3 were also used for the locomotor tests. Each subject, after receiving either 0 or 1000 ng

Table 1 Effects of morphiceptin and a pre-injection intromission on copulation in an X-maze

	Intromission latency (s)		Number intromitting		Failures to choose any goal box (% of trials)		Mean latency to female (s)		First latency to female (s)		Choice of female's goal box (% of trials)	
	Saline	Morphiceptin	Saline	Morphiceptin	Saline	Morphiceptin	Saline	Morphiceptin	Saline	Morphiceptin	Saline	Morphiceptin
Pre-injection intromission	37.2±20.2	383.8±92.8**	12	7	1.25±1.25	5.83±2.7	9.9±1.7	11.6±1.4	8.0±2.5	22.4±6.0*	93.5±3.1	95.0±2.6
No pre-injection intromission	139.2±71.3	548.3±6.4**	11	2*	1.04±1.04	8.66±3.63*	11.4±2.2	13.4±3.5	8.5±2.0	15.8±4.3	97.0±1.4	94.3±2.4

* $P<0.05$ different from saline
** $P<0.01$ different from saline

morphiceptin, was placed into a plywood box (96 cm×96 cm ×48 cm), painted grey with a taped grid on the floor, forming 16 squares. The animal was allowed to explore the grid box freely for 15 min. The number of rears (animal stands on hindlimbs) and the number of lines crossed (front two paws over a taped line) were recorded during the 15 min.

Histology and statistics

Cannula placements were verified histologically. Data from animals with cannula tips within 0.5 mm of the MPOA or within 0.5 mm of the VMH were analyzed. For copulation tests (experiment 1a), repeated measures analyses of variance and Neuman-Keuls post-hoc tests were used separately for each brain area. For the reflex tests (experiment 3), repeated measures analyses of variance and Neuman-Keuls post-hoc tests were also used. If an animal did not achieve an intromission in experiment 1 or a reflex in experiment 3, the maximal time of the study (1800 s or 1200 s, respectively) was used to calculate latency statistics. In experiment 1a, one subject mounted the female but failed to intromit her, after receiving a VMH injection; therefore, a latency of 1800 s was assigned as his intromission latency for that test. All other animals copulated to ejaculation during all tests. For locomotor tests (experiment 4) and the copulation test with naloxone (experiment 1b), correlated *t*-tests were used.

For X-maze tests (experiment 2), two-factor analyses of variance were used to compare the two drug doses (0 and 1000 ng) and the two behavioral treatments (with and without a preinjection intromission). McNemar tests were used to compare the number of animals that failed to intromit the female. Only subjects that completed all four conditions in the X-maze were used for statistical analysis. If the male failed to intromit the female on the three separate trials of 5 min (300 s) each, 900 s was used to calculate latency statistics presented in Table 1. Mount and intromission latencies were calculated based on the total time the male spent in the female's goal box prior to mount or intromission. For example, if the male intromitted 15 s into his second trial in the female's goal box, he received an intromission latency of 315 s (300 s for the first trial and 15 s for the second). Two subjects failed to mount or intromit the female in the goal box on three trials following an injection of morphiceptin; therefore, a 900-s latency was assigned for their mount and intromission latencies. Increased latencies can result both from increased latencies on trials when the male did intromit the female, and from failing to intromit her and incurring maximum latencies; therefore, uncorrelated *t*-tests were used to compare the latencies of animals that did intromit on the first exposure to the female.

Results

Experiment 1a: effects of morphiceptin in the MPOA and VMH on copulation

Morphiceptin increased the mount [$F(2,30)=8.43$, $P<0.002$] and intromission latencies [$F(2,30)=9.74$, $P<0.001$] in a dose dependent manner when injected into the MPOA (Fig. 1). The same doses of morphiceptin when injected into the VMH had no effect on these parameters [$F(2,30)=1.44$ for mount latency and $F(2,30)=0.63$ for intromission latency]. No other parameters changed significantly following a morphiceptin injection into either the VMH or the MPOA. However, there was a nonsignificant trend for the intromission ratio to be decreased by the 100 ng dose in the MPOA [$F(2,30)=3.14$, $P<0.06$], due to a large increase in the number of nonintromissive mounts. The increases in mount and intromission latencies suggest that either a motivational component or reflex component of sexual behavior was impaired.

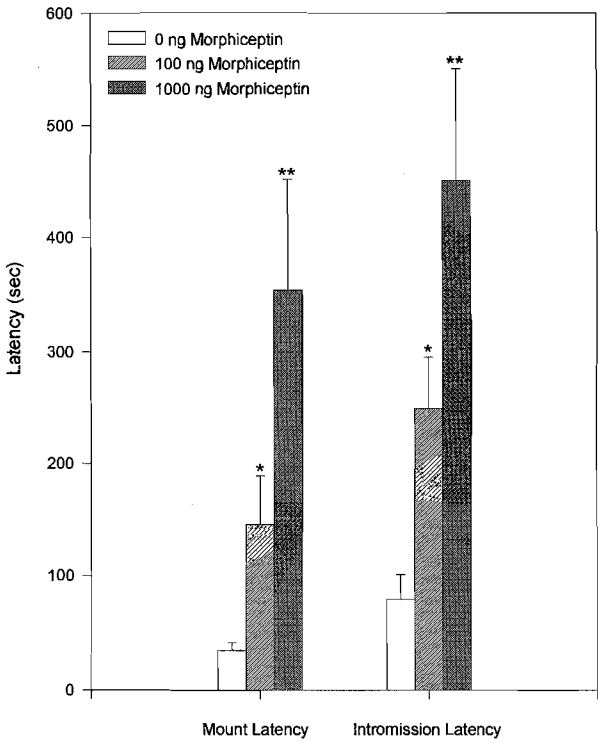

Fig. 1 Effects of injections of 0 ng, 100 ng and 1000 ng morphiceptin into the MPOA on mount and intromission latencies. *$P<0.05$, significantly different from 0 ng; **$P<0.01$, significantly different from 0 ng

Experiment 1b: effects of naloxone pretreatment

Naloxone, compared to vehicle, blocked the morphiceptin induced increase in mount and intromission latencies in male rats (mount latency: naloxone+morphiceptin, 89.52±47.58, vehicle+morphiceptin, 317.67±117.89, $t(5)=2.66$, $P<0.05$; intromission latency: naloxone+morphiceptin, 112.05±55.12, vehicle+morphiceptin, 462.17±128.05, $t(5)=3.45$, $P<0.02$).

Experiment 2: effects of morphiceptin on performance in an X-maze

Morphiceptin, compared to vehicle, significantly increased mount and intromission latencies in the X-maze [$F(1,33)=35.74$, $P<0.001$; $F(1,33)=41.96$, $P<0.001$, respectively; Table 1], similar to its effects in the copulation test. The increased intromission latency reflects both an increase in the latency of those that did intromit during the first interaction with the female [$t(6)=3.4$, $P<0.02$] and a decrease in the number of animals that intromitted on the first interaction in the absence of a preinjection intromission [$\chi^2(1)=7.11$, $P<0.05$; Table 1].

Table 2 Effects of morphiceptin on penile reflexes and general locomotion

	Reflex measures				General locomotion measures	
	Total erections	Anteroflexions	Seminal emissions	Reflex latency	No. of lines crossed	Rears
Saline	19.8±4.3	3.4±1.2	0.5±0.2	604.4±122.9	227.3±34.1	88.1±14.1
100 ng morphiceptin	22.5±5.4	3.7±1.2	0.5±0.2	775.5±116.5		
1000 ng morphiceptin	26.7±4.8	6.5±2.2	0.4±0.1	481.1±122.3	271.5±36.9	71.7±9.2

The percent choice of the female was not significantly different between the drug conditions. However, the percent of trials in which the subject did not choose any goal box increased following morphiceptin injections, compared to vehicle injections [$F(1,33)=9.57$, $P<0.05$]. The latency to reach the female's goal box for the first time also increased following morphiceptin injections [$F(1,33)=8.59$, $P<0.05$ Table 1].

Experiment 3: effects of morphiceptin on genital reflexes

There were no significant differences in any measure (Table 2).

Experiment 4: effects of morphiceptin on locomotion

There were no significant differences in the number of lines crossed in the grid box or the number of rears during the 15-min test period (Table 2).

Discussion

A microinjection of morphiceptin into the MPOA delayed the onset of copulation as shown by the increases in mount and intromission latencies in both the copulation and X-maze tests. The increase in initiation latencies was antagonized by a pretreatment with naloxone. These findings support earlier research concerning the behavioral effects of morphiceptin microinjected into the MPOA (Matuszewich and Dornan 1992). The copulation study confirms that these effects are at least somewhat specific for the MPOA, because injections of morphiceptin into the VMH had no effect on copulatory behavior. However, the explanation of this delay still has not been resolved. Neither sexual motivation, as measured in the X-maze, nor genital reflexes, as measured in the ex copula genital reflex test, were disrupted.

Male sexual behavior has been subdivided into various components (Beach 1956; Sachs 1978). While different divisions have been proposed, most factor analyses include an arousal or motivational component and a copulatory or performance component. Sachs originally proposed that an "initiation factor" corresponded to appetitive aspects of copulation and could be measured by mount and intromission latencies (Sachs 1978). Therefore, the increase in mount and intromission latencies by morphiceptin in the copulation test suggested that a motivational component may be impaired. The X-maze measured sexual motivation as the male's percent choice of the female, separate from copulation itself. However, in the X-maze task the morphiceptin did not disrupt the male's choice of the female's goal box. Thus, sexual motivation, as measured in the X-maze, was not impaired.

Previous data also suggested that opioids did not influence sexual motivation. For example, the opioid agonist β-endorphin microinjected into the MPOA disrupted the onset and duration of copulatory behavior, without affecting a measure of sexual motivation, lever pressing, using a second order schedule of reinforcement (Hughes et al. 1987, 1990). Neither β-endorphin nor the opioid antagonist naloxone injected into the MPOA prevented the establishment of a conditioned place preference when injected before the male was placed with the estrous female in a compartment (Hughes et al. 1990). On the other hand, a microinjection of naloxone into the MPOA did disrupt conditioned place preference when the reinforcing event, ejaculation, occurred directly prior to the subject being placed into the apparatus (Agmo and Gomez 1993). The opioid antagonist naloxone apparently interfered with the reinforcing properties of ejaculation and therefore the establishment of the place preference. While not all aspects of appetitive or motivated responses were tested in the X-maze, it does not appear that specifically sexual motivation was disrupted by the μ opioid injection.

Stavy and Herbert (1989) reported that if the injection of β-endorphin occurred after the first intromission, the inhibitory effects of β-endorphin were not seen; the mount, intromission and ejaculation latencies were similar to vehicle injected controls. Increased latencies were observed, however, if the male received a preinjection intromission with one female, then received a MPOA injection of β-endorphin, and was then returned to a different receptive female. The authors suggested that β-endorphin injections disrupt a transition in behavioral "states" between investigating the female and mounting her (Stavy and Herbert 1989). In the present X-maze test, intromission latency was significantly affected by two factors, the preinjection intromission and the morphiceptin. Subjects that did not receive a preinjection intromission showed an increase in intromission latency compared to subjects that did receive a preinjection intromission, regardless of drug dose: 0 or 1000 ng morphiceptin. Similarly, an injection of morphiceptin increased latency to intromit, compared to vehicle injected controls, regardless of behavioral method, i.e. absence or presence of preinjection intromission. Although the preinjection intromission affected the latency to copulate, it did not negate the effects of morphiceptin. Everitt (1990) ha

suggested that the MPOA serves to find the appropriate motor patterns for response to an incentive stimulus, in this case mounting the estrous female. Morphiceptin may disrupt the matching of the stimulus to the correct somatomotor patterns, even after the transition from investigating the female to mounting her.

The other parameters significantly affected in the X-maze following an injection of morphiceptin were an increase in the percentage of trials in which the male failed to choose any goal box and an increase in the latency to the female on the subject's first trial to her. This suggests that either locomotion or general responsiveness to motivational stimuli may have been disrupted. However, motor activity as measured in the open field apparatus was not affected by the morphiceptin injections, nor was the average latency to the female's goal box across all trials. Thus, the morphiceptin may produce a more general motivational deficit early in the test session. Percent choice of the female was calculated only for those trials on which the male actually chose a goal box. Therefore, specifically sexual motivation was unimpaired; however, a generalized responsiveness to any stimulus may be decreased. These data are in contrast to the effects of dopamine (DA) antagonists in the MPOA. We have previously reported that injections into the MPOA of various DA antagonists decreased specifically sexual motivation (percent choice of female), but did not affect measures of motor activity (Warner et al. 1991; Moses et al. 1995). Furthermore, the DA antagonist haloperidol injected into the MPOA decreased the rates of level changing by male rats in a bi-level apparatus, in search of a receptive female (Pfaus and Phillips 1991). However, it is not clear whether this deficit reflected inhibition of sexual motivation specifically, general motivational responsiveness, or locomotor activity.

In conclusion, the μ opioid agonist morphiceptin, injected into the MPOA, delayed the onset of copulatory behavior in male rats by increasing mount and intromission latencies. The increase in latencies does not appear to be caused by an erectile dysfunction, a specifically sexual motivational deficit or a locomotor deficit. Perhaps the ability to activate the specific somatomotor pattern necessary to respond appropriately within the environment may be impaired, or a more general motivational component may be inhibited.

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References

Agmo A, Gomez M (1993) Sexual reinforcement is blocked by infusion of naloxone into the medial preoptic area. Behav Neurosci 107: 812–818

Agmo A, Paredes R (1988) Opioids and sexual behavior in the male rat. Pharmacol Biochem Behav 30: 1021–1034

Band L, Hull EM (1990) Morphine and dynorphin (1–13) microinjected into the medial preoptic area and nucleus accumbens: effects on sexual behavior in male rats. Brain Res 524: 77–84

Beach FA (1956) Characteristics of masculine "sex drive". In: Jones MR (ed) Nebraska symposium on motivation vol. 4. University of Nebraska Press, Lincoln, pp 1–31

Bitran D, Hull EM (1987) Pharmacological analysis of male rat sexual behavior. Neurosci Biobehav Rev 11: 365–389

Chang KJ, Killian A, Hazum E, Cautrecasas P, Chang JK (1981) Morphiceptin (NH_4-Tyr-Pro-Phe-Pro-$CONH_2$): a potent and specific agonist for morphine (μ) receptors. Science 212: 75–77

Everitt BJ (1990) Sexual motivation: a neural and behavioural analysis of the mechanisms underlying appetitive and copulatory responses of male rats. Neurosci Biobehav Rev 14: 217–232

Hetta J (1977) Effects of morphine and naltrexone on sexual behavior of the male rat. Acta Pharmacol Toxicol 41: 53–61

Hughes AM, Everitt BJ, Herbert J (1987) Selective effects of β-endorphin infused into the hypothalamus, preoptic area and bed nucleus of the stria terminalis on the sexual and ingestive behaviour of male rats. Neuroscience 23: 1063–1073

Hughes AM, Everitt BJ, Herbert J (1990) Comparative effects of preoptic area infusions of opioid peptides, lesions and castration on sexual behavior in male rats: studies of instrumental behaviour, conditioned place preference and partner preference. Psychopharmacology 102: 243–256

Lieblich I, Baum M, Diamond P, Goldblum N, Iser C, Pick C (1985) Inhibition of mating by naloxone or morphine in recently castrated, but not intact male rats. Pharmacol Biochem Behav 22: 361–364

Matuszewich L, Dornan WA (1992) Bilateral injections of a selective μ-receptor agonist (morphiceptin) into the medial preoptic nucleus produces a marked delay in the initiation of sexual behavior in the male rat. Psychopharmacology 106: 391–396

McIntosh T, Vallano M, Barfield R (1980) Effects of morphine, β-endorphin and naloxone on catecholamine levels and sexual behavior in the male rat. Pharmacol Biochem Behav 13: 435–441

Moses J, Loucks JA, Watson HL, Matuszewich L, Hull EM (1995) Dopaminergic drugs in the medial preoptic area and nucleus accumbens: effects on motor activity, sexual motivation and sexual performance. Pharmacol Biochem Behav 51: 681–686

Mumford, L, Kumar, R (1979) Sexual behaviour of morphine-dependent and abstinent male rats. Psychopharmacology 65: 179-185

Myers B, Baum M (1979) Facilitation by opiate antagonists of sexual performance in the male rat. Pharmacol Biochem Behav 10: 615–618

Pfaus J, Gorzalka, B (1987) Opioids and sexual behavior. Neurosci Biobehav Rev 11: 1–34

Pfaus J, Phillips AG (1991) Role of dopamine in anticipatory and consummatory aspects of sexual behavior in the male rat. Behav Neurosci 105: 727–743

Sachs BD (1978) Conceptual and neural mechanisms of masculine copulatory behavior. In: McGill TE, Dewsbury DA, Sachs BD (eds) Sex and behaviour. Plenum Press, New York, pp 267–295

Stavy M, Herbert J (1989) Differential effects of β-endorphin infused into the hypothalamic preoptic area at various phases of the male rat's sexual behaviour. Neuroscience 30: 433–442

Van Furth WR, Van Emst MG, Van Ree JM (1995) Opioids and sexual behavior of male rats: involvement of the medial preoptic area. Behav Neurosci 109: 123–134

Warner RK, Thompson JT, Markowski VP, Loucks JA, Bazzett TJ, Eaton RC, Hull EM (1991) Microinjection of the dopamine antagonist cis-flupenthixol into the MPOA impairs copulation, penile reflexes and sexual motivation in male rats. Brain Res 540: 177–182