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Methadone Reduces Sexual Performance and Sexual Motivation in the Male Syrian Golden Hamster

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MURPHY, M R *Methadone reduces sexual performance and sexual motivation in the male Syrian golden hamster* PHARMAC. BIOCHEM BEHAV. **14**(4) 561–567, 1981.—The debilitating effect of opiate drugs on sexual function has been known clinically for hundreds of years but has become a topic of experimental investigation only recently. The purpose of the current study was to examine the effects of the opiate drug methadone and the opiate blocking drug naltrexone on the sexual behavior of male hamsters. Methadone, administered at dosages of 1, 2, 4, 8, and 16 mg/kg, was found to cause a dose related decline in measures of both sexual performance and sexual motivation, with measures of sexual performance being the more sensitive to the drug. The debilitating effect of methadone was judged to be highly selective for sexual behavior since, for example, at 16 mg/kg of methadone, sexual behavior was eliminated but ambulatory activity was unaffected. Pretreatment with naltrexone blocked the effects of methadone and posttreatment reversed the effects, thereby indicating that the methadone was inhibiting sexual behavior by acting on specific opiate receptors. The results demonstrate that the male hamster is an excellent small animal model for use in studying the mechanisms of opiate induced sexual dysfunction and further support the hypothesis that the endogenous opiates may be involved in the regulation of sexual behavior

Opiates Methadone Naltrexone Sexual behavior Reproduction Hamsters

THE DEBILITATING effect of opiate drugs on sexual function has been known for hundreds of years. In 1563, Garcia d'Orta wrote that contrary to popular belief, the use of opium did not improve sexual function but, rather, was likely to lead to total impotence [7]. Today it is recognized that the use of opiate drugs by men can cause depressed libido, impotence, delayed ejaculation, decreased sexual pleasure, elimination of sexual dreams, decreased nocturnal emissions, reduced ejaculate volume, and reduced sperm motility (e.g., [1, 3, 5, 12, 14, 22]). In male opiate addicts, withdrawal can cause premature ejaculation, spontaneous erection and ejaculation, and recovery of sexual motivation and performance [22]. Use of opiates by women can prevent orgasm, depress libido, and cause amenorrhea and infertility [3, 5, 14]. In female addicts, withdrawal can cause sexual hypersensitivity and increased vaginal secretion [22].

In contrast to the long established and extensive information on the effects of opiate drugs on human sexual function, there is relatively little data on the effects of opiates on the mating behavior of experimental animals. The first studies on this topic were published in 1974 and 1975 [2,4] and demonstrated that acute administration of morphine, and to a lesser extent methadone, decreased sexual activities in male monkeys (*Macaca nemestrins*). More recently, the discovery of the endogenous opiates has led to increased interest in the effects of opiates on sexual function and to speculation that the endogenous opiates may be involved in the regulation of sexual behavior and reproduction. Such speculation has been the impetus to studies that have demonstrated that the sexual behavior of male rats is reduced or eliminated by an acute injection of morphine [10,15], by addiction to morphine [15,24], by intraventricular injection of D-Ala-Met-enkephalinamide [6] or beta-endorphin [13]. Furthermore, there have been reports that opiate antagonists have direct effects on sexual behavior [6, 10, 19, 20, 23], including a dramatic facilitation of copulatory behavior in otherwise non-copulatory male rats [6]. There also have been reports that levels of endogenous opiates in brain and blood are altered during copulatory activity [19,23].

The possible involvement of the endogenous opiates in sexual function further is indicated by the facts that opiate receptors are found in the vas deferens [8], the muscular vessel which conveys spermatozoa from the epididymis to the posterior urethra for ejaculation, and in the central nervous system projection areas of the vomeronasal system [9], a chemosensory system which has been implicated in reproduction [26]. Also, opiate immunoreactive cell bodies have been reported to exist in the preoptic area [11], a brain area

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which has long been known to be involved in the control of sexual behavior.

The purpose of the present study was to examine the effects of the common opiate agonist methadone on the sexual behavior of the male hamster, a species that has proven useful in the investigation of the mechanisms of sexual behavior [17,18]. In order to determine if the effects of methadone are mediated by specific opiate receptors, an examination also was made of the ability of the opiate antagonist naltrexone to reverse or prevent the effects of methadone. In an attempt to improve on the behavior recording methods used in earlier studies, a detailed analysis of sexual behavior was performed by using a computer-based event recorder.

EXPERIMENT 1: EFFECTS OF METHADONE ON SEXUAL BEHAVIOR AND FERTILITY

METHOD

Subjects

All subjects were descended from wild hamsters *(Mesocricetus auratus)* captured in Syria in 1971 [16]. Subjects were born at the NIMH, weaned at about 3 weeks of age, isolated into separate plastic cages at about 5 weeks of age, and used in the present experiments at 20–30 weeks of age. They received NIH Rat Ration and water ad lib and occasional sunflower seeds and apple. The hamsters were kept on a reversed 16/8 hour, light/dark cycle. Prior to the start of the experiment, all males had displayed normal copulatory behavior during each of two 30-minute opportunities to mate with a receptive female. Sixty female hamsters in natural estrus served as sexual partners for the males.

Behavioral Testing—Sexual Behavior

The testing chamber was a clear Plexiglas cylinder 25 cm high and 30 cm in diameter which sat on a clear sheet of glass. To start a mating test, a male and female hamster were placed inside the cylinder on the glass. A mirror at 45 degrees below the glass afforded a ventral view of the copulating pair and allowed for greater precision in measuring certain behavior patterns. Testing was conducted under dim red illumination during the dark phase of the light/dark cycle. Tests of the same hamster were at least 5 days apart. A standard test length of 30 minutes was chosen because this time is sufficient for most male hamsters to complete all the ejaculations they will have with one female, and yet is short enough to avoid postcopulatory aggression by the female.

An event recorder was programmed on a small computer so that a push of any key on a standard keyboard caused the identity of that key and the time it was pushed to be entered into computer memory and later stored on a computer disk. The following behavior patterns were recorded and analyzed with respect to (a) frequency, (b) total duration, (c) latency, and (d) average duration of each activity: (1) lick female's genitalia, (2) mount with incorrect orientation, (3) mount from rear but without intromission (i.e., mount only), (4) mount with intromission, (5) intromit with a single intravaginal thrust (ST intromission), (6) intromit with multiple intravaginal thrusts (MT intromission), (7) ejaculate, (8) lick own genitalia, (9) sniff female's head, (10) sniff female's body, (11) bite female, (12) attack female, (13) fight with female, (14) groom self, (15) scent mark, and (16) ignore the female In addition, the ejaculatory latency (EL) (time between the first intromission in a series and the next ejaculation), postejaculatory interval (PEI) (time between an ejaculation and the next intromission), and frequency of preceeding intromissions in the series were computed for each ejaculation Four compound measures were analyzed: (a) total mating activity, i.e., the sum of all time engaged in behavior patterns 1 through 8 listed above; (b) all intromissions, i.e., the sum of the frequency of behavior patterns 5, 6, and 7; (c) sniff female, i.e., the time engaged in behavior patterns 9 and 10; and (d) hit rate, i.e., the percentage of all correctly oriented mounts which resulted in intromission. (Since a "correctly oriented mount" was recorded only when the male vibrated his penis against the vulva or perineum, hit rate measures ability to gain penile erection and vaginal insertion rather than ability to locate the vaginal orifice.)

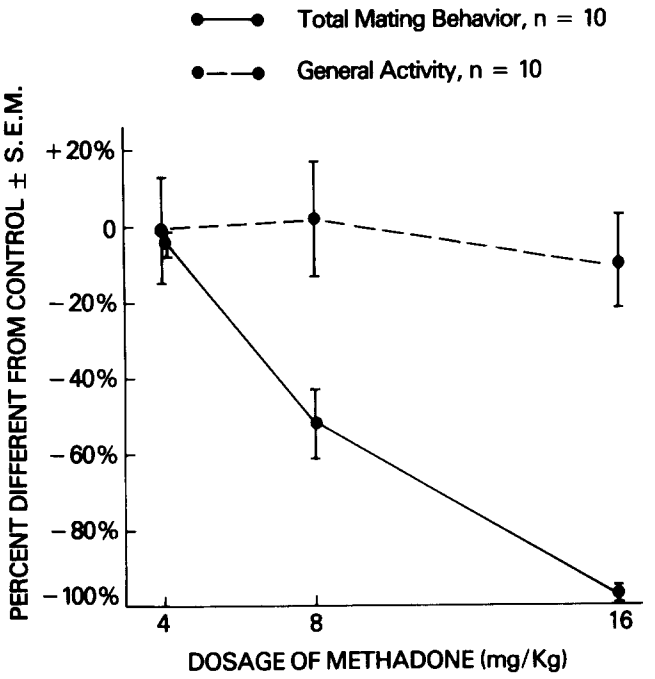

FIG. 1 A comparison of the effects of methadone on total mating behavior and on general ambulatory activity

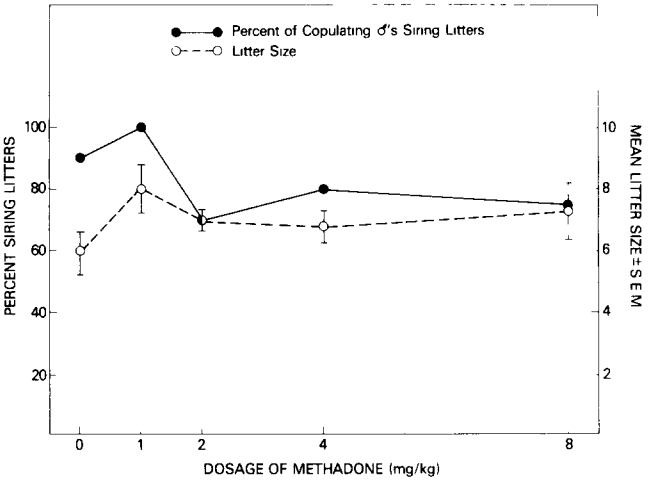

FIG. 2 Effect of methadone on fertility

Analysis resulted in up to 100 quantitative measures of behavior per test. (The acutal number of measures depended on the frequency of ejaculations.) The data from multiple tests were combined into groups according to the dosage of methadone, and the groups were compared using one-way analysis of variance for repeated measures. In order to determine the dosage at which significant change first occurred, data collected at each dose level were compared with control data using the William's test [25].

To save space and simplify discussion, the results of only 19 measures of behavior will be presented in detail (see Tables 1 and 2). Each of these measures was selected because it met at least one of the following criteria: (1) it is a meaningful or unique measure of hamster copulatory behavior; (2) it uniquely illustrates the effects of methadone on sexual behavior; or (3) it commonly is used in studies on rodent copulatory behavior.

Behavioral Testing—Activity

To determine if changes in general activity could account for the effects of methadone on sexual behavior, the ambulatory activity of an additional 10 male hamsters was measured after injection of saline control, 4, 8, and 16 mg/kg of methadone using an Opto-Varimex (Columbus Instruments) activity monitor. Except for the male being alone, the testing procedures used for the activity measurement were identical to those used for recording sexual behavior.

Drug Treatments

Ten male hamsters were each tested for sexual behavior after injection of saline control, 1, 2, 4, or 8 mg/kg of Methadone hydrochloride (Lilly), given in a different sequence for each subject in order to minimize the possibility of order effects, and after 16 mg/kg methadone, given after tests with all other dosages had been completed. Methadone was diluted with saline and administered in a volume of 10 ml/kg, except for the 16 mg/kg dose which was administered at 16 ml/kg. Methadone was injected IP 30 minutes before the start of testing for both the mating and the activity measurements.

Assessment of Fertility

In order to determine if copulatory aberrancies produced by methadone affected male fertility, females mated with experimental males were followed to term (16 days), at which time the presence or absence of a litter and the litter size were recorded.

RESULTS AND DISCUSSION

The effects of methadone on the 19 selected measures of sexual behavior are presented in Table 1.

While both sexual performance and sexual motivation declined with increasing dosage of methadone, sexual performance was the more sensitive to the drug. For example, sexual performance, as measured by hit rate, was reduced significantly by only 2 mg/kg of methadone but sexual motivation, as measured by total mating activity, did not show a significant decline until the 8 mg/kg dosage. Other measures of performance, such as the ejaculatory latency and the number of intromissions required for ejaculation, were significantly affected at the 4 mg/kg dosage of methadone, but measures of motivation, such as total frequency of mounts with intromissions and the latency to the first single thrust intromission, were not affected significantly until the 8 mg/kg dosage.

At the 2 and 4 mg/kg dosages of methadone, mounts without intromissions were significantly increased, and, consequently, hit rate was decreased, thereby indicating that methadone reduces the ability to gain penile erection and intromission. At 4 mg/kg the average duration of intromission and the average duration of licking own genitalia were significantly decreased, further suggesting an effect of low doses of methadone on the penis directly or on neural mechanisms of penile sensitivity or erection. The possibility of a specific and sensitive effect of opiates on the genitalia is supported also by the recent report that administration of morphine to female hamsters causes a dose related decrease in the magnitude of the lateral displacement of the perineum in response to perivaginal tactile stimulation [21].

Both licking of the female's genitalia and sniffing the rest of the female's body were affected in a complicated manner by methadone, tending to increase at the 8 mg/kg dosage and then decrease at the 16 mg/kg level. The finding that nonsexual social behavior (i.e., sniffing the female) was increased at the same dose (8 mg/kg) at which sexual behavior was severely decreased suggests that methadone was having a specific effect on sexual motivation as opposed to having a general effect on social behavior.

The total time spent licking own genitalia decreased with increasing dosage of methadone whereas self grooming of the head and body increased. This contrast in the effects of methadone on two self-manipulatory behaviors, one clearly sexual and the other of a more general nature, suggests a specific action of methadone on sexual behavior rather than some general action on sensation or motor control.

For the 0, 1, 2, and 4 mg/kg dosages, all males achieved at least one intromission; at the 8 mg/kg dosage, 3 of the 10 males failed to intromit, and at the 16 mg/kg dosage, no male intromitted. However, even when no copulation occurred, males still investigated and licked the females, albeit at a reduced level. This small amount of stimulation was sufficient to keep most female partners in lordosis and prevent any aggression toward the males.

A comparison of the effects of methadone on ambulatory activity with its effects on total mating activity (Fig. 1) indicates that a depression of activity cannot account for the sexual effects of methadone, even at the highest dose of the drug used in this experiment.

In spite of aberrancies in sexual performance after 2 and 4 mg/kg of methadone and a severe reduction in ejaculation frequency after 8 mg/kg, the percent of males siring litters and the mean litter size were unaffected for those males that did copulate (Fig 2) Thus, for the measures used here, a single injection of methadone did not affect fertility.

EXPERIMENT 2: EFFECTS OF NALTREXONE ON METHADONE INDUCED SEXUAL DYSFUNCTION

To determine if methadone was affecting sexual behavior by acting on opiate receptors, the ability of naltrexone, a specific opiate antagonist, to reverse or prevent the effects of naltrexone was tested.

METHOD

The subjects were 30 male hamsters identical in characteristics to the hamsters used in Experiment 1 Testing procedures were the same as those used in Experiment 1.

To determine if naltrexone (naltrexone hydrochloride,

TABLE 1

EFFECTS OF METHADONE ON THE SEXUAL BEHAVIOR OF MALE HAMSTERS

Behavior	Measure	Dosage of Methadone (mg/kg) 0	1	2	4	8	16	F (*df*) $p<$
Total Mating	Dur.	1078 2	1098 0	1166.4	1036 8	518 4*	36.0*	87 03(5,45)
	SEM	43 2	30.6	41 4	37 8	104.4	19 8	0 001
Mount Only	Freq.	16.1	27 7	47 7*	49 1*	30.3	0.0	7 51(5,45)
	SEM	3 8	8.5	10.5	6 0	9.3	0 0	0 001
All Intromissions	Freq.	72 1	73.8	75.9	61.6	17 1*	0 0*	46.29(5,45)
	SEM	5.3	5 7	8.3	6.4	4 1	0 0	0 001
ST Intromission	Freq	37.8	36 0	43.7	45 2	15 8*	0 0*	15 74(5,45)
	SEM	5.8	2.8	8.8	4 1	3 9	0 0	0 001
ST Intromission	Lat	53 3	108.8	83.4	187 0	478.0*	—	3 44(4,24)
	SEM	10 6	48.9	19.6	81 2	181 3		0.025
ST Intromission	AD	1 7	1 6	1.6	1.5	1 6	—	1 59(4,24)
	SEM	0 1	0 1	0.1	0 1	0 1		ns
MT Intromission	Freq	26 1	30.0	24.7	9.9*	0 0*	0.0*	15 72(5,45)
	SEM	3 2	4 9	5 1	5 6	0 0	0 0	0.001
MT Intromission	Lat	682.9	755 6	824.9	1208 7*	—	—	5.41(3,18)
	SEM	103 5	74 4	117.7	155 8			0.01
MT Intromission	AD	5 0	4 0	3 5	2 6*	—	—	4 77(3,18)
	SEM	0 7	0 4	0.5	0 2			0 025
Hit Rate	%	82 7	75.4	63 2*	55.5*	34.4*	—	14 75(4,28)
	SEM	3 2	6 5	5 9	4 9	6.4		0 001
Ejaculate	Freq.	8 1	7 8	7.6	6 3	1.2*	0.0*	51 03(5,45)
	SEM	0 9	0 5	0.7	0 9	0.6	0 0	0 001
EL for EJ no 1	Lat	77 0	86.5	114.1	287.2*	—	—	5 77(3,27)
	SEM	11 6	16 5	20.2	82 4			0 005
PEI for EJ no 1	Dur.	33 2	42 0	33 9	46 7*	—	—	3 29(3,27)
	SEM	2 4	2 8	3 3	5 1			0 05
Intros to EJ no. 1	Freq	8 5	9.4	11 3	16 2*	—	—	2.80(3,27)
	SEM	1 0	1 4	2 3	3.4			ns
Lick Own Genitals	Dur	618 6	593 0	586.7	518 8	227 0*	1.6*	68 36(5,45)
	SEM	33 8	33 1	32.6	33 3	56 2	0.6	0.001
Lick Own Genitals	AD	5 3	5 1	4 3	4.2	3 9	—	4 26(4,36)
	SEM	0.3	0 6	0.4	0.2	0 5		0 01
Lick F's Genitals	Dur.	81 5	93 9	94 0	123 2	125 7	35.0	6 33(5,45)
	SEM	19 9	16 8	19 1	22 1	19.5	19 8	0 001
Sniff Female	Dur	342.1	315 3	251.1	261.8	436 4	174 5*	4 35(5,45)
	SEM	38 6	32.1	27 1	27 6	68 4	55 0	0 005
Self Groom	Dur.	181.8	197.6	194.7	250 9	266.1	470.2*	4 35(5,45)
	SEM	29 9	26.1	13 7	36 7	25 9	108.6	0 005

Methadone was administered 30 minutes before the start of a 30 minute test. Statistical comparisons were made between saline and each of the drug conditions using the William's test [25]. For *, $p<0.01$; otherwise, $p>0$ 01. See Methods for a description of the behaviors and measures. Dur , Lat., and AD (average duration) are in seconds SEM=Standard Error of the Mean.

TABLE 2

EFFECTS OF METHADONE, NALTREXONE OR A COMBINATION OF BOTH DRUGS ON THE SEXUAL BEHAVIOR OF MALE HAMSTERS

		Drug Treatment			
Behavior	Measure	Saline	Methadone	Naltrexone	Combination
Total Mating	Dur	1089 4	346 5§	994.3†	1013.2
	SEM	25 4	107 1	32 6	43 9
Mount Only	Freq	26 0	15.2	6 7‡	18 1
	SEM	5 6	6 5	1 9	3 6
All Intromissions	Freq	74.4	13 0§	56 5†	61 3†
	SEM	4 5	5 6	2 7	3.0
ST Intromission	Freq.	35 9	11 7†	24.0*	29.9
	SEM	6.0	5.0	2.0	3.5
ST Intromission	Lat	37 8	562 3	67.4†	102 3
	SEM	5 1	263 5	8 2	37 8
ST Intromission	AD	1 7	1 7	1 9*	2.0§
	SEM	0.1	0.1	0.1	0.1
MT Intromission	Freq.	29.8	0.0§	26.4	25.5
	SEM	2.9	0.0	2.1	3 0
MT Intromission	Lat	671 4	—	574.9	756.4
	SEM	51.2		42 7	62.5
MT Intromission	AD	3.9	—	4.7*	3 9
	SEM	0 3		0.6	0 4
Hit Rate	%	75 8	45.5*	90.3‡	78.4
	SEM	4.5	9 6	2.3	4.1
Ejaculate	Freq.	8.7	1 3§	6 1§	5.9§
	SEM	0.4	0 8	0.6	0.5
EL for EJ no 1	Lat	70 5	113.2	54.3	105 5
	SEM	14.3	20 1	9.4	28 2
PEI for EJ no. 1	Dur	42 6	46 5	46.4	55.5‡
	SEM	4 3	1 0	1 3	5.2
Intros to EJ no 1	Freq	7.5	9.8	5.6	9 4
	SEM	1 0	1.3	0.7	2.3
Lick Own Genitals	Dur.	639.5	177.8§	647 3	605.2
	SEM	28 7	59.6	38.3	23.5
Lick Own Genitals	AD	5.1	4 7	6 4†	5.8†
	SEM	0.3	0 8	0.4	0 2
Lick F's Genitals	Dur.	55.5	80.1	57 8	67.8
	SEM	9 6	20.4	10.7	14.4
Sniff Female	Dur.	233.0	282.2	268 1	289.1†
	SEM	23 3	38.4	19 3	23.5
Self Groom	Dur	266 6	387.7*	243 3	210.9†
	SEM	28 2	69.4	27.7	16.6

Naltrexone was administered 1 hour before the test and methadone was administered 30 minutes before the test. Tests of sexual behavior were 30 minutes long Statistical comparisons were made between saline and each of the drug conditions using a Student's t-test. For *, $p<0$ 05, †, $p<0.02$; ‡, $p<0.01$; and §, $p<0.001$, otherwise, $p>0.05$. See Methods for description of behaviors and measures. Dur , Lat., and AD (average duration) are in seconds SEM=Standard Error of the Mean

Endo Laboratories lot B221P65) could reverse the mating-inhibiting effects of methadone, 20 male hamsters were each administered 16 mg/kg of methadone and observed, one at a time, with an estrous female for 30 minutes. The males were then removed from the test chamber and 10 of them were injected with 20 mg/kg of naltrexone and 10 with saline control (both injections given IP). They immediately were returned to the test chamber and were observed until an intromission occurred, or for a maximum time of 15 minutes

To determine if naltrexone could prevent the effects of methadone on mating behavior, 10 additional male hamsters were each tested after receiving (1) an injection of 20 mg/kg naltrexone followed by an injection of 8 mg/kg of methadone; (2) saline followed by saline; (3) saline followed by 8 mg/kg methadone; and (4) 20 mg/kg naltrexone followed by saline. In each case the first injection was given 60 minutes before testing, and the second injection was given 30 minutes before testing. The four conditions were administered in a different sequence for each subject to reduce the possibility of order effects. Naltrexone was dissolved in 0 9% saline and administered in a volume of 1.0 ml/kg.

RESULTS

None of the 20 males made any attempt to copulate following an injection of 16 mg/kg of methadone. The 10 males that then received naltrexone began to show increased social and sexual interest in the female within 60 seconds of the injection and began to copulate within 120 seconds. Five of the 10 males that received saline following the methadone briefly licked the female's genitalia (mean latency of 312.4 sec.), but none of them made any attempt to copulate during the 15 minute observation period. Since the latency to first intromission for saline treated controls is about 40 seconds (see Tables 1 and 2), these results suggest that the 20 mg/kg of naltrexone took about 80 seconds to reverse the mating inhibiting effects of 16 mg/kg of naltrexone.

Table 2 presents the effects of methadone, naltrexone, and a combination of both drugs on the sexual behavior of male hamsters. Methadone was found to significantly affect 8 of the 19 behaviors reported. Six of these significant effects were prevented by pretreatment with naltrexone. The other two effects, decreased frequency of all intromissions and decreased frequency of ejaculations, were partially prevented by naltrexone. However, it should be noted that naltrexone given alone had a significant effect on both of these behaviors and that both effects were in the same direction as those produced by methadone given alone. Thus, it is possible that the behavioral change observed after the drug combination was not due to a failure of the naltrexone to prevent fully the effect of methadone but was the result of the naltrexone exerting its own effect over that of methadone. This possibility is further suggested by the finding that naltrexone given alone was significantly different from the control condition for 10 behavioral patterns, but was significantly different from the naltrexone+methadone condition on only two behaviors. For both of these behaviors, mounts and hit rate, the effects of naltrexone were restored to control levels by the combination with methadone. Thus, in these instances, it might be said that methadone blocked the effects of naltrexone A more detailed analysis and discussion on the effects of naltrexone on the mating behavior of male hamsters will be the subject of a separate paper (Murphy, in preparation).

GENERAL DISCUSSION

The results of the experiments reported here indicate that an acute injection of methadone causes a dose related decline in both the sexual performance and the sexual motivation of male hamsters, with the effects on the sexual performance occurring at lower dosages than the effects on sexual motivation. However, for those males that mated, fertility was not affected. For several reasons (a decrease in sexual behavior concurrent with no affect on activity or non-sexual social interest, and a decrease in genital grooming concurrent with an increase in body and head grooming), the results indicate that the opiate methadone has a highly specific effect on sexual behavior. The ability of the opiate antagonist naltrexone to reverse or prevent the mating-inhibiting effects of methadone indicates that these effects are being mediated by specific opiate receptors

Although there are no data on the effects of acute administration of opiates on the sexual behavior of men without a history of opiate abuse, the effects of acute administration of methadone on the mating behavior of hamsters has several similarities to the reported effects of opiate addiction on human sexual function. First, at the higher doses of methadone there was a reduction and eventual elimination of all sexual behavior in male hamsters (Fig. 1), which might be comparable to loss of libido reported for opiate use by men. Second, starting at the 2 mg/kg dosage and becoming more severe at higher dosages, the hamster displayed an impaired ability to gain erection and vaginal intromission (Table 1), a condition which might be comparable to the impotence observed in opiate addicted men Third, the increase in ejaculation latency seen in the methadone treated hamster (Table 1) might be similar to the delay of ejaculation commonly reported after opiate use by human males. Thus, the hamster, while displaying a considerably different copulatory pattern from that of the human, may be a suitable small animal model for investigating some aspects of opiate induced sexual dysfunction.

The results obtained in the current studies on the effects of acute methadone on the sexual behavior of male hamsters are generally consistent with the results previously obtained following administration of opiate peptides or morphine in rats. Intraventricular injections of both the synthetic opiate peptide D-Ala-Met-enkephalinamide [6] and the natural opiate peptide beta-endorphin [13] have been shown to produce a dose related decline in sexual behavior of male rats without significant changes in other social behavior [6,13] or in activity or eating [6], indicating, along with the results of the current study, that sexual function is highly and specifically sensitive to opiates. Similarly, morphine has been found to induce a dose related decline in the mating behavior of rats [10,15]. Unfortunately, differences in the copulatory patterns of rats and hamsters as well as differences in behavioral analysis make detailed comparisons between the results of the rat and hamster studies difficult.

The current results contribute to a steadily increasing body of evidence indicating that the endogenous opiates may be fundamentally involved in the regulation of sexual behavior and in the etiology of sexual dysfunction.

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