

Sociosexual Behaviors of Female Rats During and After Chronic Treatment With the Sympatholytic Agent Guanethidine

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EMERY, D. E. *Sociosexual behaviors of female rats during and after chronic treatment with the sympatholytic agent guanethidine*. PHARMACOL BIOCHEM BEHAV 23(2) 267-273, 1985.—Ovariectomized female rats were chronically administered saline or guanethidine sulfate, a drug that blocks adrenergic neurons and, when chronically administered, results in peripheral sympathectomy. The females were periodically injected with estradiol benzoate and progesterone and tested for sexual behaviors before, during and after the six-week period of daily guanethidine or saline injections. Tests for copulatory behavior included tests for lordotic responsiveness to manual stimulation and tests of sociosexual behaviors displayed by the females in a complex testing environment. The complex environment permitted the test females to control their coital contacts with sexually active males and their interactions with sexually inactive males and ovariectomized female rats. Guanethidine treatment did not alter lordotic responsiveness to manual stimulation but did reduce the frequency of copulatory acts engaged in by the females in the complex environment. During the first test in the complex environment following the start of drug injections, the guanethidine-treated females, in comparison to saline-treated females, displayed a lower frequency of lordotic behavior during coital contacts. The changes in behavior produced by the sympathetic drug, guanethidine, implicate the autonomic nervous system in the regulation of copulatory pacing in the female rat.

Sociosexual behavior Guanethidine Sympathectomy

THE role of the autonomic nervous system in reproduction in the gonadally intact female rat has been examined with several surgical and chemical techniques but the endpoints considered have been functional ones, such as successful pregnancy, that only indirectly reflect a behavioral competence for copulatory behavior following damage to components of the autonomic nervous system. One of the earliest studies of autonomic function in reproduction involved examination of the effects of surgical sympathectomies upon the induction of pseudopregnancy following mechanical cervical stimulation or copulation with male rats [15]. The early research appeared to indicate that abdominal sympathectomy, with some parasympathetic damage, led to an inability of female rats to become pseudopregnant following mechanical stimulation but permitted a continued competence for pseudopregnancy following mating [15]. Further research has indicated that the parasympathetic pelvic nerves are necessary for induction of pseudopregnancy by either mechanical stimulation or mating and that extensive abdominal sympathectomy is compatible with normal pregnancy [6]. Another component of the parasympathetic system, the vagus, has also been implicated in the control of the estrous cycle and induction of pseudopregnancy [4].

Since surgical intervention disrupts sensory fibers also, the use of drugs to produce chemical sympathectomies offers the advantage of damaging only the sympathetic fibers. Production of a chemical sympathectomy with administration of 6-hydroxydopamine did not alter estrous cycles or induction

of pregnancy in female rats but did reduce the number of live births [22]. Thus sympathectomy does not appear incompatible with copulation when the female rats are tested in the typical laboratory situation in which they cannot avoid contact with sexually active males.

The purpose of the present study was to examine directly the changes in copulatory behavior that may result from chronic administration of an adrenergic-neuron blocking drug, guanethidine, to female rats. Guanethidine sulfate is a guanidium adrenergic-blocking agent that also produces irreversible destruction of cell bodies of sympathetic neurons [5, 11, 18]. Administration of guanethidine, unlike other methods of chemical sympathectomy, produces permanent destruction of sympathetic neurons in adults, as well as newborns, and does not produce damage in central noradrenergic neurons [19]. In the rat chronic treatment with high dosages of guanethidine sulfate (10-20 mg/kg, daily) results in morphological, biochemical and functional indications of total sympathectomy that persist for at least three to six months [18,19]. The magnitude of sympathetic damage is related to dosage and the dosage used in the present experiment produces maximal effects on sympathetic function in the rat [19,20].

Ovariectomized female rats in the present study received chronic (6 week) treatment with daily injections of guanethidine sulfate. The females were repeatedly tested, during and after the drug treatment period, for a conventional measure of feminine copulatory behavior, the lordosis

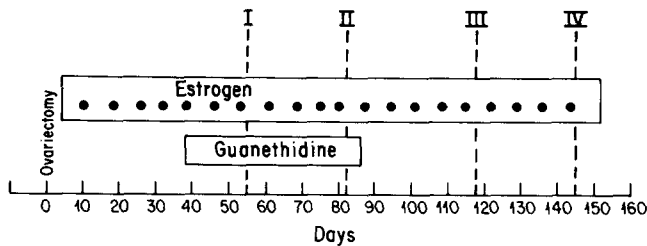


FIG. 1. Diagram of sequence of hormone and drug administration and behavioral tests starting with day of ovariectomy as Day 0 of experiment. Days of behavioral tests in the complex environment are denoted by Roman numerals. Days on which estradiol benzoate was administered are indicated by solid circles within the box marked "Estrogen." Guanethidine sulfate or saline vehicle was administered daily during the period indicated by the box labeled "Guanethidine."

quotient, and for a measure of the pacing of coital contacts by the females. The lordosis quotient was computed from responses of the test females to manual stimulation.

Female rats pace their coital contacts dependent upon the quality of the stimulation that they receive during the contact [23]. To measure the pacing of copulation it is necessary to provide the female with a test situation in which she controls her proximity to copulating males. In the present report females were tested in a large complex environment that allowed the females to control their contacts with several types of stimulus animals: sexually active males; sexually inactive males; and ovariectomized females without hormone replacement.

It has previously been demonstrated that lesions in hypothalamic areas, implicated in autonomic control, alter the pacing of copulation in the female rat [9]. In the present experiment, it was hypothesized that manipulation of autonomic function might disrupt the relatively sensitive process of copulatory pacing but leave the ability to display lordotic behavior unchanged. In the complex environment pacing is measured by the frequency of copulatory acts received by the female and is related to the amount of interaction between the test female and the sexually active males. The behavioral measures that reflect the nature of these interactions are the duration and frequency of visits by the test females to the sexually active males and the display of avoidance behaviors by the females while with the sexually active males. The preference of test females for proximity to sexually passive males versus stimulus females is related to hormonal state [8] and was examined in the present study. Measures of lordosis were also obtained from the complex-environment-tests.

METHOD

Twenty-two Long Evans (Charles River, Wilmington, MA) female rats were received at 60 days of age and housed in unisexual groups in wire rack cages. They were maintained on a 12:12 hr light/dark schedule with lights off at 1200 hr. Food and water were continuously available.

Three days after arrival the females were bilaterally ovariectomized under Metofane (Pittman Moore) anesthesia. Eleven days after ovariectomy the females received their

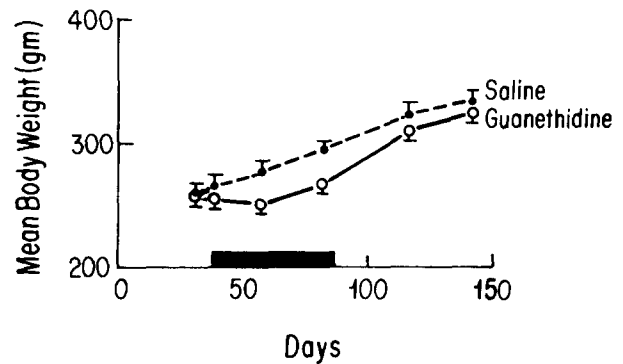


FIG. 2. Mean body weight of guanethidine- and saline-treated females before, during and after drug treatment. Day 0 is day of ovariectomy. The drug period during which females received daily injections of guanethidine or saline is indicated by the solid bar on the abscissa. Bar extensions indicate 1 SEM.

first injection, SC, of estradiol benzoate (EB). Two days after the EB injection each female received a 500 μ g progesterone (P) injection, SC, in a 5 mg P/ml solution of olive oil. This sequence of EB and P injections was continued throughout the experiment at intervals of 7–9 days. Figure 1 depicts the intervals between estrogen injections during the course of the experiment. On the first two days of estrogen injection each female was given 13.3 μ g EB in a 133 μ g EB/ml solution of olive oil. For the third and all subsequent estrogen injections the dosage of EB was 10 μ g EB/kg body weight in a 10 μ g EB/ml solution of olive oil.

Behavioral tests were conducted 4–5 hr after the P injections and occurred during the first half of the females' dark period. The females were normally tested for lordosis to manual stimulation but occasional tests of behavior in a complex environment were also conducted immediately after the test female's responses to manual stimulation had been observed. The behavioral data from four of the tests in the complex environment are included in the present report. The dates of the four reported tests are indicated in Fig. 1. The tests were separated by approximately monthly intervals and the first test reported was the first test of the females in the complex environment.

Following the first four hormonal sequences of EB and P and their associated manual stimulation tests, the females were randomly assigned to receive either guanethidine (GUAN) or vehicle (saline; SAL) treatment. The day before the fifth EB injection, the guanethidine or saline injections were started. The injections, IP, were made between 1200 and 1400 hr each day. Guanethidine sulfate (Ismelin, Ciba) was administered in a 40 mg/kg dosage in a 13.33 mg/ml solution of 0.9% NaCl and was adjusted to pH 7.5–8. The vehicle injection of saline was equal volume. The guanethidine and saline injections were continued daily throughout the 6 week period indicated in Fig. 1.

BEHAVIORAL TESTING PROCEDURE

Tests for lordosis to manual stimulation were conducted in a 10 gal aquarium with wood shavings on the floor of the aquarium. The test female was stimulated by placing the palm of the experimenter's hand on the back of the test female with the index and middle fingers, separated by the

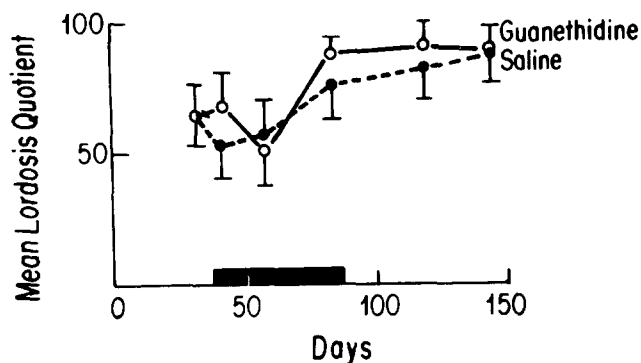


FIG. 3. Mean lordosis quotient of guanethidine- and saline-treated females before, during and after drug treatment. Day 0 is day of ovariectomy. The drug period during which females received daily injections of guanethidine or saline is indicated by the solid bar on the abscissa. Bar extensions indicate 1 SEM.

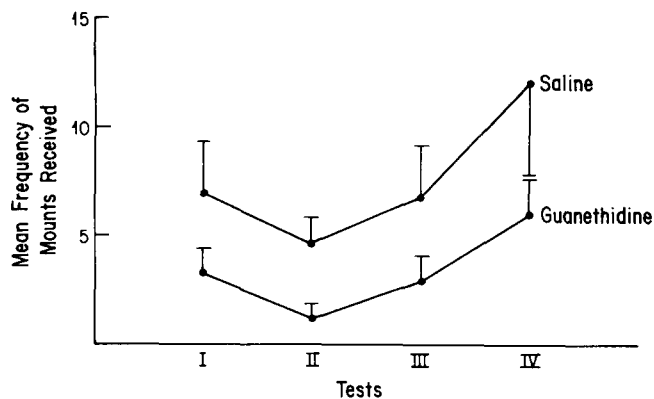


FIG. 4. Mean frequency of mounts received by the guanethidine- and saline-treated females during the drug (Tests I and II) and post-drug (Tests III and IV) phases of the experiment. Days that the tests occurred are indicated in Fig. 1. Bar extensions indicate 1 SEM.

test female's tail, applying rhythmic stimulation to the perigenital region and the thumb and other fingers stimulating the flanks of the test female. These stimulations were applied every 15 sec for a 5 sec duration until 10-5 sec stimulations had been applied to the test females. The testing was videotaped and examined for the presence of lordosis in the test female. Lordosis, both in the manual stimulation test and the complex environment, was scored when the test female became immobile and displayed elevation of the nose and hindquarters. The weakest lordosis scored was a posture of the female in which the top of the head and back were parallel to the floor. The frequency that the female displayed lordosis to stimulation was determined, divided by 10 (the number of stimulations), and the resulting number multiplied by 100 to produce the measure termed lordosis quotient (LQ).

The complex environment used in the present experiment consisted of three large circular arenas interconnected by an elevated passageway. The clear Plexiglas arenas were 60 cm in diameter and 45 cm high and each was connected to the passageway by its own three-step staircase (see [8], for greater detail). During behavioral testing one arena contained 3-5 sexually active males. Males were replaced when they ejaculated or slowed in copulation. The second arena contained three sexually passive males who had received bilateral lesions in the medial preoptic area. The passive males would investigate the test females but would not engage in copulatory acts. The last arena contained three ovariectomized (OVX) female rats with no hormone replacement. Only the test females were allowed free entry to and egress from the arenas. The stimulus animals were rapped on the nose with a dowel rod whenever they attempted to leave their arenas.

On the day preceding the first test in the complex environment, the test females were adapted for approximately 1 hr in a three-arena apparatus without stimulus animals present. Ten min before each behavioral test in the three-arena apparatus, each test female was placed in a barren complex environment for a 10 min adaptation period. The test females were then placed in the interconnecting passageway of a three-arena apparatus with all stimulus animals present and behaviors were scored for 10 min by an observer using an Esterline Angus event recorder.

During testing the following behaviors were scored: the

copulatory acts of the active males and the accompanying lordotic or passive rejection behaviors of the test female; active rejection behaviors of the test female; and the occurrence of the stereotyped posture of posing in which the test female orients her hindquarters toward the stimulus animal(s). The copulatory acts of the sexually active males are mounts, intromissions and ejaculations. Passive rejection is scored when the female allows the male to mount but the female makes nonlordotic movement during the male's copulatory act. Active rejection behaviors consist of the test female either rolling onto her back or fending with her forepaws in response to mount attempts by the active male(s). The test female may also avoid coital contacts by remaining under the bottom step of the staircase in the active male arena. A derived measure of lordotic ratio (LR) was computed and is defined as (the frequency of lordotic postures associated with masculine copulatory acts divided by the total number of masculine copulatory acts) \times 100.

RESULTS

Within 24 hr of the first guanethidine injection all of the GUAN females displayed ptosis, a condition that persisted for the rest of the experiment. The GUAN females, when handled the day following their first guanethidine injection, also appeared qualitatively less active than the SAL females and did not struggle when being injected. One GUAN female appeared ill with acute respiratory difficulties following two days of guanethidine treatment and one SAL female developed respiratory problems between Tests II and III. The data from both females were eliminated from statistical comparisons.

Mean body weights of the GUAN (=10) and SAL (=10) females through the course of the experiment are presented in Fig. 2. The groups did not differ in body weight on the day of the last EB injection preceding guanethidine injections nor did they differ at the time of the first EB injection following the onset of guanethidine injections. (Student's *t*-test for both comparisons). Data for the LQ of the two groups of females in response to manual stimulation are presented in Fig. 3. As for body weight there were no significant differences between the two groups on LQ before or three days following the start of guanethidine injections (Student's *t*-test

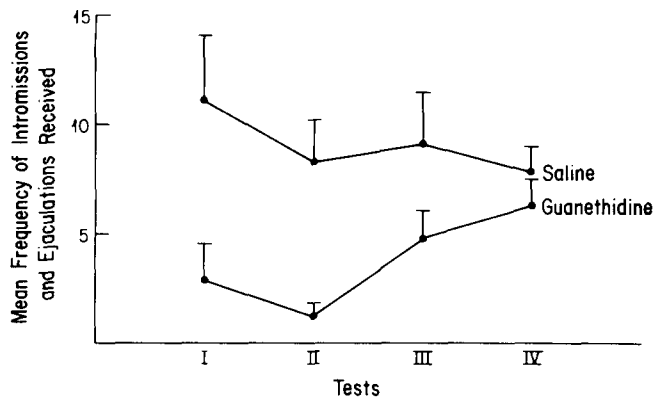


FIG. 5. Mean frequency of intromissions and ejaculations received by the guanethidine- and saline-treated females during the drug (Tests I and II) and post-drug (Tests III and IV) phases of the experiment. Days that the tests occurred are indicated in Fig. 1. Bar extensions indicate 1 SEM.

for all comparisons). All subsequent statistical comparisons, except where indicated, were made with $2 \times 2 \times 2$ analyses of variance with repeated measures on two factors. The repeated measures were the Periods of the experiment (Drug and Post-drug) and the Tests within the periods (first and second reported tests of each period).

Analysis of variance of the body weight data for the weights two days before each of the reported tests in the complex environment indicated both Period and Test main effects, $F(1,18)=357.2$, $p<0.001$, and $F(1,18)=159.3$, $p<0.001$, respectively, indicating a progressive increase in weight for both groups. There was also a significant Drug \times Period interaction, $F(1,18)=6.58$, $p<0.05$, reflecting the relative retardation of weight gain for the GUAN females during the Drug period. The sum of body weights for Tests I and II when compared between the GUAN and SAL females indicated that the SAL females were heavier than the GUAN females (Student's t -test; $t(18)=2.92$, $p<0.01$). The groups did not differ significantly when their sum of weights for Tests III and IV were compared.

Analysis of the LQ measure revealed main effects of Period, $F(1,18)=8.05$, $p<0.05$, and Test, $F(1,18)=9.89$, $p<0.01$, and a Period \times Test interaction, $F(1,18)=14.59$, $p<0.005$. Against the progressive increase in the LQ measure over testing, the interaction effect indicates the greater rate of increase in LQ for the Drug Period. Comparisons of LQ collapsing over drug treatment groups (GUAN and SAL) indicated that the females significantly increased on the LQ measure between Tests I and II (paired t -test; $t(19)=3.69$, $p<0.005$) but not between Tests III and IV.

Data for the frequency of mounts received by the females during the four tests in the complex environment are presented in Fig. 4. Analysis of variance indicated a significant Drug effect, $F(1,18)=4.79$, $p<0.05$; a Period main effect, $F(1,18)=4.59$, $p<0.05$, and a Period \times Test interaction, $F(1,18)=7.34$, $p<0.05$. The GUAN females engaged in fewer mounts than the SAL females and there was an increase for both groups in the mount frequency between the periods. The Period \times Test interaction indicates the relative stasis in the mount frequency (MF) measure over the first two tests in contrast to the increment in MF occurring between Tests III and IV in the Post-drug period. Comparisons of MF, collaps-

ing over drug treatment, indicated no significant change in MF between Tests I and II but the increase between Tests III and IV approached significance (paired t -test; $t(19)=2.04$, $p=0.053$).

The mean frequencies of intromissions and ejaculations received during the four tests are presented in Fig. 5. Again there was a significant Drug effect, $F(1,18)=10.05$, $p<0.01$, indicating that the GUAN females received fewer intromissions and ejaculations in comparison to the SAL females. There was also a Drug \times Period interaction, $F(1,18)=4.49$, $p<0.05$, reflecting approach of the GUAN females toward control levels of intromission and ejaculation frequency (IEF) during the Post-drug period. Comparisons, between drug treatment groups, of the sum of IEF for tests within the periods indicated that the GUAN females received fewer intromissions and ejaculations than the SAL females during the Drug period (Student's t -test; $t(18)=3.38$, $p<0.005$) but the groups did not differ significantly during the Post-drug period.

Data for the duration and frequency of entries to each of the three arenas are presented in Figs. 6 and 7, respectively. For the measure of duration in the active male arena the Drug main effect only approached significance, $F(1,18)=4.39$, $p<0.10$, however, there was a Period \times Test interaction, $F(1,18)=4.45$, $p<0.05$. Collapsing over drug treatment, the comparison of Tests I and II indicated that the females displayed a significant decline in the duration spent with the active males (paired t -test, $t(19)=2.27$, $p<0.05$) and no significant difference between III and IV. There was a significant Drug effect, $F(1,18)=4.75$, $p<0.05$, on the frequency of entries to the active male arena indicating the lower frequency of entries for the GUAN females in comparison to the SAL females. On this behavioral measure there were also Period and Test main effects, $F(1,18)=26.28$, $p<0.001$; $F(1,18)=11.87$, $p<0.01$, respectively, reflecting the gradual increase in frequencies of entry to the active male arena for both groups over testing.

In addition to exits from the active male arena, there are other possible means of avoiding copulatory contacts in the complex testing apparatus: hiding under the bottom step and active rejection of the sexually active males. During Test I a few females from each treatment group displayed active rejection for less than 10 sec each and one GUAN female displayed active rejection for 55 sec. Several females of both groups displayed under-step behavior in the active male arena with all of them spending less than 25 sec under the step except for one GUAN female who stayed under the step for 227 sec. There was no effect of drug treatment on the display of these avoidance behaviors, indeed, by Test II the behaviors were rarely shown and both groups of females chiefly paced their coital contacts by avoiding the active male arena.

Analyses of variance for the durations and frequencies of entry in the passive male and OVX female arenas revealed no Drug effects but significant Period main effects on the frequency of entry measure for both the passive male, $F(1,18)=21.28$, $p<0.001$, and OVX female arenas, $F(1,18)=18.20$, $p<0.001$. There was also a significant Test main effect for frequency of entry to the OVX female arena, $F(1,18)=6.78$, $p<0.05$. These effects indicated the gradual increase in the frequency of entries over testing for both treatment groups. For the duration in the passive male arena, the ANOVA also revealed a significant Period \times Test interaction, $F(1,18)=4.58$, $p<0.05$. The interaction reflected the increase in duration spent in the passive male arena that

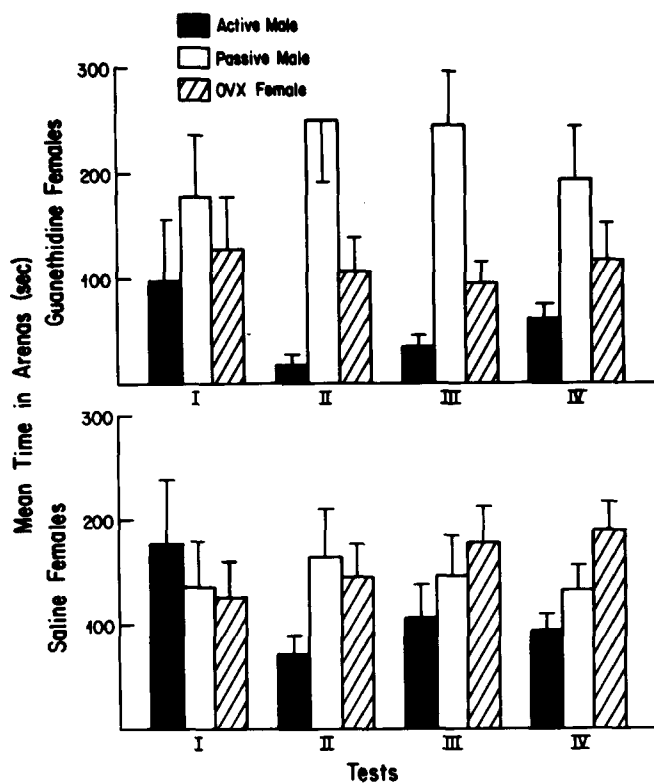


FIG. 6. Mean time spent in each of the three large arenas by the guanethidine- and saline-treated females during the drug (Tests I and II) and post-drug (Tests III and IV) phases of the experiment. Days that the tests occurred are indicated in Fig. 1. Bar extensions indicate 1 SEM.

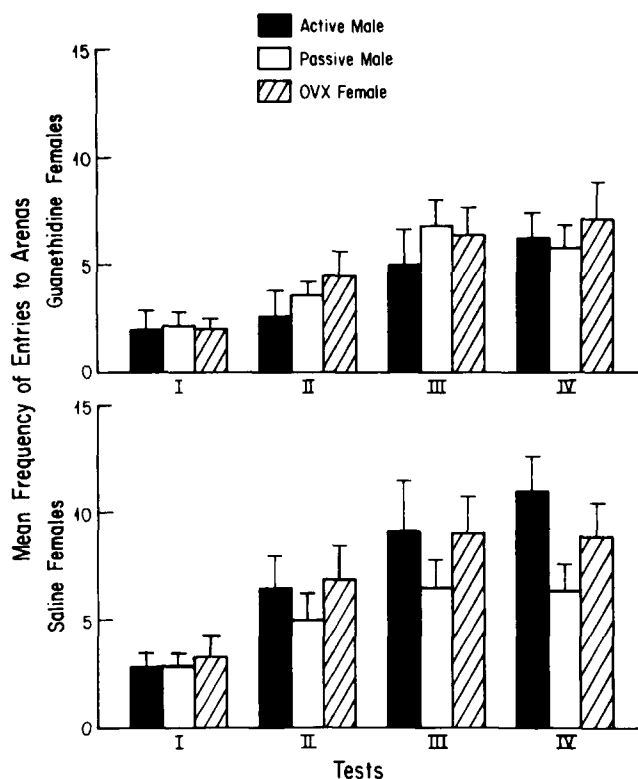


FIG. 7. Mean frequency of entries into the three large arenas by the guanethidine- and saline-treated females during the drug (Tests I and II) and post-drug (Tests III and IV) phases of the experiment. Days that the tests occurred are indicated in Fig. 1. Bar extensions indicate 1 SEM.

occurred between Tests I and II. Comparisons with the paired *t*-test, collapsing over treatment groups, did not indicate that these differences between tests within periods were significant.

A priori planned comparisons were also made to examine the preference of the test females for proximity to the passive males in comparison to the OVX females. Paired *t*-tests for the durations spent with the passive males and OVX females were performed for each group on each test. Only the GUAN females on Tests II, $t(9)=5.49, p<0.005$, and Test III, $t(9)=2.30, p<0.025$, displayed a significant preference in seeking proximity to passive males rather than OVX females.

Data for the total frequency of poses displayed are presented in Table 1. Analysis of the pose frequency measure indicated a Period \times Test interaction, $F(1,18)=4.44, p<0.05$, reflecting the high pose frequency for both groups on Test II.

Data for the mean LR for each of the tests are presented in Table 1. Since an LR is only computed for an animal when they receive at least one copulatory act, the number of females for which an LR can be computed varies from test to test, and consequently, a Student's *t*-test was used to analyze the LRs of each test. Only on Test I did the treatment groups differ with the GUAN females displaying a significantly lower mean LR than the SAL females, $t(15)=3.18, p<0.005$. On all the mounts of Test I during which the GUAN and SAL females failed to display lordosis, the test females displayed passive rejection.

DISCUSSION

Guanethidine treatment did not alter the behavior of the females on a standard test of feminine copulatory behavior (the lordotic frequency to manual stimulation), however, the drug treatment did influence reproductive behavior when the females were tested in a situation that allowed them to pace their contacts with stimulus animals. In the complex environment the GUAN females engaged in fewer mounts and intromissions plus ejaculations in comparison to the SAL females. The GUAN females entered the active male arena less frequently than the SAL females.

There is evidence for some biochemical and functional recovery following chronic treatment with the dosage of guanethidine used in the present experiment which may be due both to a loss of the acute pharmacological effects of guanethidine following cessation of guanethidine treatment and to a possible regeneration from actual structural damage to cells. Recovery continues from the first to the third month following cessation of guanethidine treatment and the recovered physiological functions remain stable thereafter [19]. There was evidence of some recovery of function on the intromission plus ejaculation frequency measure between the Drug and Post-drug periods of the present study. The GUAN females did not differ from the SAL females in the frequency of intromissions plus ejaculations received during the Post-drug portion of the study. Due to the fluctuations between tests in the number of animals that received coital

TABLE 1
MEANS (\pm S.E.M.) OF THE LORDOTIC RATIO AND POSE FREQUENCY DISPLAYED BY
FEMALES DURING THE FOUR TESTS IN THE COMPLEX ENVIRONMENT

Treatment	Behaviors							
	Lordotic Ratio				Pose Frequency			
	Tests				Tests			
	I	II	III	IV	I	II	III	IV
Guanethidine								
Mean	45.8	100.0	96.4	83.0	8.3	22.5	11.3	9.4
S.E.M.	20.8	0.0	2.0	5.3	3.8	9.2	4.4	3.3
n	6	5	9	10	10	10	10	10
Saline								
Mean	94.3	97.1	100.0	89.6	9.6	17.3	10.0	8.1
S.E.M.	2.9	1.6	0.0	2.9	2.7	7.4	2.3	2.6
n	10	9	9	10	10	10	10	10

acts, the lordosis measure in the complex environment was evaluated with *t*-tests rather than with an analysis of variance. There was not a general influence of GUAN treatment on the LR measure but rather an influence of the drug on the first test of the Drug Period. The specificity of the LR change to the first test could have been due to temporal changes in physiological responses to the drug treatment. An alternative hypothesis arises from the observation that both groups of females had reductions from Test I to Test II in the duration spent with the active males. During the first test in the complex environment both the GUAN and SAL females appeared relatively inefficient in pacing the frequency and intensity of coital contacts. At the first test rather than using absence from the active male arena to pace contacts, the females used more proximal strategies such as movement before and during the coital contact to modify the intensity of completeness of the coital contacts. Thus, the display of a lowered lordotic ratio was not consistently related to drug treatment but was associated with changes in the behavioral strategies used in pacing coital stimulation. A lowered LR could have contributed to the GUAN females' reduction of intromissions plus ejaculations received on the first test since the female's assumption of the lordotic posture is necessary for penile insertion into the vagina.

The within-group comparisons of durations spent in the passive male and OVX female arenas revealed that only the GUAN females displayed a significant preference for the passive male arena and then only on Tests II and III. The GUAN females provide a distinct contrast to the behavior of ovariectomized female rats receiving estrogen treatment without progesterone. The EB-alone females, as the GUAN females, engage in few coital contacts, however, the EB-alone females display a preference for proximity to the stimulus females when tested in the complex environment [8]. It should be noted that Tests II and III were also the tests during which the GUAN females spent the shortest duration with the active males suggesting that the GUAN females may have found some aspects of contact with gonadally intact males attractive and may have spent more time with the passive males to compensate for their brief durations in the active male arena. The EB-alone females apparently find any

contact with gonadally intact male rats relatively undesirable [8].

As previously observed with this dosage of guanethidine [19], ptosis persisted following cessation of guanethidine treatment, however, body weight differences did not persist in the present study. Ptosis, following sympathetic damage, is related to paralysis of the smooth muscle of Horner in the upper eyelid [12]. The surviving GUAN females appeared in good health throughout the experiment, however, their general levels of muscle tension when being handled seemed qualitatively reduced.

The effects of guanethidine treatment appear to be principally upon the peripheral nervous system with no evidence for changes in central noradrenergic activity following systemic treatment nor is tyrosine hydroxylase activity altered in the adrenals with the present dosage [19]. The mechanisms through which altered autonomic activity might influence copulatory pacing can be examined from three perspectives: (1) integrity of balance within the autonomic nervous system (ANS); (2) potential specificity of organ systems affected; and (3) the nature of proximal mechanisms affected by altered ANS activity. Firstly, it is possible that any imbalance in function between sympathetic and parasympathetic portions of the autonomic nervous system may alter copulatory pacing in the female rat. It is certainly premature to interpret the present data as indicating that the activity of sympathetic neurons increases the frequency of copulatory contacts sought by female rats. Regarding the second concern, the present technique can not discern if sympathetic innervation to specific tissue/organ systems is crucial to produce the observed disruption of pacing. Lastly, there are potential mechanisms by which alterations in the ANS might influence copulatory pacing. One such mechanism is through changes in sensory processing. Sensory information concerning the quality and intensity of peripheral stimulation contributes to the pacing of copulatory contacts by female rats [2,10]. The ANS may influence both sensory systems [14] and skeletal muscle activity [3], in addition to its direct control of visceral and vascular systems.

The likelihood that the behavioral effects of guanethidine administration are mediated through its sympatholytic action

provides a cautionary note when interpreting the behavioral results of other experimental manipulations that affect autonomic functioning. The effects of systemic administration of noradrenergic drugs upon feminine copulatory behavior appear to be complex and, at present, inconsistent using traditional measures of feminine copulatory behavior in the rat [1, 7, 13]. Isolation of noradrenergic manipulations to the central nervous system (CNS) still leaves open the possibility that it is the alteration in the CNS regulation of autonomic balance that is crucial for the behavioral effects of the experimental manipulations. Hypothalamic areas, in particular, receive noradrenergic innervation [17] and have been implicated in both the control of autonomic function [16] and the control of feminine sexual behavior (for a review, [21]). Demonstration of reduced sympathetic activity following lesions of the ventromedial hypothalamus (VMH) [24]

and recent work in the present laboratory indicating that VMH lesions produce some of the behavioral effects observed with chronic administration of guanethidine [9] point to the possibility that VMH lesions may influence feminine copulatory behavior partially through effects upon the autonomic nervous system.

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REFERENCES

1. Ahlenius, S., J. Engel, H. Eriksson, K. Modigh and P. Sodersten. Involvement of monoamines in the mediation of lordosis behavior. In: *Sexual Behavior: Pharmacology and Biochemistry*, edited by M. Sandler and G. L. Gessa. New York: Raven Press, 1975, pp. 137-145.
2. Bermant, G. and W. H. Westbrook. Peripheral factors in the regulation of sexual contacts by female rats. *J Comp Physiol Psychol* **61**: 244-250, 1966.
3. Bulbring, E. and J. H. Burn. The sympathetic vasodilator fibres in the muscles of the cat and dog. *J Physiol (Lond)* **83**: 483-501, 1935.
4. Burden, H. W., I. E. Lawrence, Jr., T. M. Louis and C. A. Hodson. Effects of abdominal vagotomy on the estrous cycle of the rat and the induction of pseudopregnancy. *Neuroendocrinology* **33**: 218-222, 1981.
5. Burnstock, G., B. Evans, G. J. Gannon, J. W. Heath and V. James. A new method of destroying adrenergic nerves in adult animals using guanethidine. *Br J Pharmacol* **43**: 295-301, 1971.
6. Carlson, R. R. and V. J. DeFeo. Role of the pelvic nerve vs. the abdominal sympathetic nerves in the reproductive function of the female rat. *Endocrinology* **77**: 1014-1022, 1965.
7. Davis, G. A. and R. Kohl. The influence of alpha-receptors on lordosis in the female rat. *Pharmacol Biochem Behav* **6**: 47-53, 1977.
8. Emery, D. E. and R. L. Moss. p-Chlorophenylalanine alters pacing of copulation of female rats. *Pharmacol Biochem Behav* **20**: 337-341, 1984.
9. Emery, D. E. and R. L. Moss. Lesions confined to the ventromedial hypothalamus decrease the frequency of coital contacts in female rats. *Horm Behav* **18**: 313-329, 1984.
10. Emery, D. E. and J. Whitney. Effects of vaginocervical stimulation upon sociosexual behaviors of female rats. *Behav Neural Biol* **43**: 199-205, 1985.
11. Eranko, L. and O. Eranko. Effects of guanethidine on nerve cells and small intensely fluorescent cells in sympathetic ganglia of newborn and adult rats. *Acta Pharmacol Toxicol (Copenh)* **30**: 403-416, 1971.
12. Everett, N. B. *Functional Neuroanatomy*, 6th edition, Philadelphia: Lea and Febiger, 1971, p. 250.
13. Everitt, B. J. Cerebral monoamines and sexual behavior. In: *Handbook of Sexology*, vol 2, edited by J. Money and H. Musaph. New York: Elsevier, 1977, pp. 429-448.
14. Freeman, B. and M. Rowe. The effects of sympathetic nerve stimulation on responses of cutaneous pacinian corpuscles in the cat. *Neurosci Lett* **22**: 145-150, 1981.
15. Haterius, H. O. Partial sympathectomy and induction of pseudopregnancy. *Am J Physiol* **103**: 97-103, 1933.
16. Hess, W. R. *Functional Organization of the Diencephalon*. New York: Grune and Stratton, 1957.
17. Jacobowitz, D. M. Fluorescence microscopic mapping of CNS norepinephrine systems in the rat forebrain. In: *Anatomical Neuroendocrinology*, edited by W. E. Stumpf and L. D. Grant. Basel: Karger, 1975, pp. 368-380.
18. Jensen-Holm, J. and P. Juul. Ultrastructural changes in the rat superior cervical ganglion following prolonged guanethidine administration. *Acta Pharmacol Toxicol (Copenh)* **30**: 308-320, 1971.
19. Johnson, E. M., Jr., and F. O'Brien. Evaluation of the permanent sympathectomy produced by the administration of guanethidine to adult rats. *J Pharmacol Exp Ther* **196**: 53-61, 1976.
20. Juul, P. and O. Sand. Determination of guanethidine in sympathetic ganglia. *Acta Pharmacol Toxicol (Copenh)* **32**: 487-499, 1973.
21. Komisaruk, B. R. The nature of the neural substrate of female sexual behavior in mammals and its hormonal sensitivity: Review and speculations. In: *Biological Determinants of Sexual Behavior*, edited by J. B. Hutchison. New York: John Wiley, 1978, pp. 349-393.
22. MacDonald, E. J. and M. M. Airaksinen. The effect of 6-hydroxydopamine on the oestrus cycle and fertility of rats. *J Pharm Pharmacol* **26**: 518-521, 1974.
23. Peirce, J. and L. Nuttall. Self-paced sexual behavior in the female rat. *J Comp Physiol Psychol* **54**: 310-313, 1961.
24. Vander Tuig, J. G., A. W. Knehans and D. R. Romsos. Reduced sympathetic nervous system activity in rats with ventromedial hypothalamic lesions. *Life Sci* **30**: 913-920, 1982.