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Microinjection of the dopamine antagonist cis-flupenthixol into the MPOA impairs copulation, penile reflexes and sexual motivation in male rats

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Microinjection of the dopamine antagonist cis-flupenthixol into the medial preoptic area was previously shown to impair male rat copulatory behavior. The present experiments provide further evidence of cis-flupenthixol's inhibitory effects on male sexual behavior. Following microinjections of moderate to high doses of cis-flupenthixol, males exhibited slower copulatory rates and fewer ejaculations in copula, fewer ex copula erections and penile movements, and reduced sexual motivation in an X-maze. Locomotion in the X-maze was not significantly affected. Microinjections of the inactive isomer trans-flupenthixol produced no change in any behavioral measure, indicating that cis-flupenthixol's effects were receptor mediated. We suggest that dopamine receptors in the MPOA influence copulation primarily by regulating reflexive and motivational factors, but not locomotion.

INTRODUCTION

Systemically administered dopamine agonists have facilitated male sexual behavior in both rodents and men[2–4,8–10,13,20,21,24,29,30,34]. Dopamine antagonists, on the other hand, have inhibited male sexual behavior when administered systemically[2,5,20].

One site of dopaminergic influence on sexual behavior is the medial preoptic area (MPOA). The MPOA is critical to the expression of male sexual behavior in all vertebrate species studied[11,15,22,23,32] and receives dopaminergic input via the A-14 incertohypothalamic tract[7]. We have shown that microinjections of the dopamine agonist apomorphine into the MPOA increased several measures of copulatory rate and efficiency[18]. We have also reported that microinjections of high doses (20 μg and 40 μg) of the dopamine antagonist cis-flupenthixol into the MPOA reduced the number of males initiating copulation and slowed its rate in those that did copulate[27]. A lower dose of cis-flupenthixol (10 μg), while having no effects on its own, did block the facilitative effects of apomorphine. Neither apomorphime nor cis-flupenthixol affected locomotion, feeding, or drinking in the home cage[27].

One means by which DA activity in the MPOA may regulate copulatory behavior is by altering genital reflexes. It is difficult to observe such reflexes during copulation; however functionally similar reflexes may be observed in restrained supine rats[14,31]. Within 10 min after retraction of the penile sheath, spontaneous erections and penile movements (anteroflexions of the penis, sometimes referred to as 'flips') can usually be observed. Systemic administration of moderate doses of apomorphine has been shown to increase the total number of penile reflexes displayed in rats[6,12,25,33]. Recently, Pehek, Thompson and Hull[26] reported that apomorphine microinjected into the MPOA, in doses that facilitated copulation, increased the number of erections and penile movements.

The following experiments were designed to: (1) test the effects of a dose of cis-flupenthixol midway between the previously ineffective 10 μg dose and the 20 μg dose, which abolished copulation in numerous animals; (2) test whether cis-flupenthixol's effects were receptor mediated by including a 20 μg dose of the inactive isomer trans-flupenthixol; (3) assess the effects of cis- and trans-flupenthixol on the ex copula display of penile reflexes; and (4) assess possible locomotor and motivational effects of cis-flupenthixol on X-maze performance.

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MATERIALS AND METHODS

Sixty adult male Long–Evans rats (300–350 g), purchased from Blue Spruce Farms (Altamont, NY), were singly housed in a temperature- and humidity-controlled environment with a 14 h light–dark cycle, lights off at 11.00 h. Twenty animals were used in each of 3 experiments. Food and water were available ad libitum. Animals were handled daily, allowing microinjections to be accomplished without anesthesia.

Surgery and cannulae

Male rats were anesthetized with ketamine hydrochloride (50 mg/kg) and xylazine hydrochloride (4 mg/kg) i.m., prepared for surgery, and placed in a Kopf stereotaxic frame with incisor bar set 5 mm above the interaural line. Animals in each study received one guide cannula aimed at, and ending 1 mm above, the left MPOA (AP 2.4, ML 0.2, DV −7.0)[28]. The skull was exposed and a small hole was drilled above the MPOA. Prior to lowering the guide cannula, 4 additional holes (one in each bone surrounding bregma) were drilled and implanted with screws, which provided anchorage for the cannula assembly. The guide cannula was lowered to the appropriate depth, and dental cement was spread around the screws and guide cannula. An obturator prevented entry of foreign material into the cannula. Details of cannula construction are described in Hull et al.[18]. In addition, the suspensory ligament was excised in all animals given ex copula genital reflex tests in order to facilitate the continuous exposure of the glans penis from the penile sheath.

At the time of drug delivery, the obturator was replaced with the injection cannula, which was connected via polyethylene tubing to a Harvard infusion pump. The rate of infusion was 1 μl/min with the injection cannula remaining in place for an additional 60 s. Behavioral testing began 5 min later.

Drugs

Cis- and trans-flupenthixol (generously donated by H. Lundbeck A/S, Copenhagen, Denmark) were dissolved in vehicle immediately prior to each testing session. The vehicle for each experiment was 1 μl sterile water.

Procedures

All testing was done during the dark period of the light–dark cycle, between 11.00 and 17.00 h. Copulatory and X-maze behavior were assessed under dim red light. Ex copula tests were done under normal illumination.

Copulatory behavior tests. Each male's home cage served as the testing arena for copulatory behavior. Males received 3 weekly preoperative tests and one postoperative baseline test. Five weekly drug tests were then conducted, with each animal receiving all doses in counterbalanced order. Each test lasted for 30 min following the first vaginal intromission, or for a total of 30 min, if no intromission occurred. The frequency and latency of mounts, intromissions, and ejaculations were recorded using a program for the IBM-XT[16]. A mount was scored when the male approached the female from the rear, clasped her flanks and performed a series of rapid, shallow thrusts. Intromissions were distinguished from mounts by the presence of a deep thrust followed by a rapid, springing dismount. Ejaculations were distinguished from mounts and intromissions by a deeper thrust followed by a prolonged grasp, slow dismount, and a 5–10 min period of inactivity. The following measures were recorded: mount and intromission latencies (times from the introduction of the female to the first mount and intromission); ejaculation latency (time from the first intromission to the first ejaculation); interintromission interval (ejaculation latency divided by number of intromissions preceding ejaculation); post ejaculatory interval (time from ejaculation to the first intromission of a new series); numbers of mounts and of intromissions preceding each ejaculation; intromission ratio (100 × intromissions/(mounts + intromissions); and number of ejaculations per test.

Penile reflex tests. Prior to ex copula tests, all rats were habituated 3 times to a restraining device consisting of a metal tube, 8.5 × 5.5 × 20.0 cm, fastened to a plate of plexiglas. This device allowed restraint of each rat in a supine position, with the lower body exposed.

Penile reflexes were evoked by retracting the penile sheath. These responses occurred in clusters, separated by 15 s or more. Within a cluster, usually 2–6 reflexes were observed. Two classes of reflexes occurred, erections and penile movements ('flips'). Three gradations of erections were scored: E1, engorgement of just the base of the glans; E2, tumescence involving both the base and the tip of the glans; E3, engorgement of the base as well as intense flaring of the tip of the glans, so that the diameter of the tip was greater than that of the base of the glans (also termed a cup). Penile movements (anteroflexions) were classified as 'short' or 'long.' A movement was classified as a 'long flip' if the penis traveled past the line perpendicular to the rat's body. Occasionally a seminal emission was observed.

Animals were given 20 min to begin a display of reflexes. A test lasted 15 min from the first reflex (i.e. an erection or penile movement). Animals were used only if they displayed reflexes on two baseline tests. Five weekly drug tests were then conducted, with each animal receiving all doses in counterbalanced order.

During experimental tests, the time of the first reflex, as well as the numbers and types of erections and penile movements were recorded with the aid of an Esterline-Angus event recorder. If a seminal emission was present upon sheath retraction, it was removed and included in the number of seminal emissions per test. A cluster was defined as any display of penile reflexes separated by 15 s or longer. Measures derived from the data included: the latency to the first reflex, the number of clusters, the intercluster interval (the avg. time between clusters), the number of seminal emissions, the total number of reflexes, the numbers of erections and penile movements, and the numbers of E1s, E2s, E3s (cups), short flips and long flips.

X-maze tests. Possible impairments of locomotion and sexual motivation were assessed by recording running speed to goal boxes of an X-maze, and percentage of trials on which the male chose the goal box containing a receptive female, respectively. The X-maze was constructed of plywood, painted gray, with a goal box at the end of each of the 4 arms. Each arm, excluding goal box, was 15.24 cm wide and extended 30.48 cm from a 15.24 × 15.24 cm central hub, the goal box (30.48 × 30.48 cm) was recessed to one side and was separated from the alley by a Plexiglas door, which could be raised to admit the male into the goal box. A length of black electrical tape was placed across the alley even with the near end of the goal box. If the male crossed this line with both of his front paws, the door was raised and he was allowed to enter. If he failed to enter, he was gently pushed into the goal box. A female was in one goal box, a

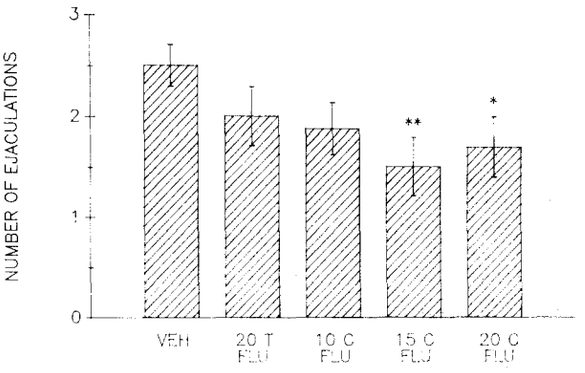

Fig. 1. Total number of ejaculations per 30 min test following microinjection of vehicle (VEH), 20 μg/μl trans-flupenthixol (T FLU), 10, 15 or 20 μg/μl cis-flupenthixol (C FLU). Values are means ± standard errors. (*$P < 0.05$, **$P < 0.01$).

TABLE I

Effects of vehicle, trans- and cis-flupenthixol microinjections into the MPOA on masculine sexual behavior, Expt. 1

Values are means ± S.E.M. for: #E's (All), number of ejaculations for all animals; #E's (E), number of ejaculations for males that ejaculated; # males E, number of males that ejaculated; EL (All), ejaculation latency for all animals (includes 1800 sec for those that did not ejaculate); EL (E), ejaculation latency for males that ejaculated; III (E), interintromission interval for males that ejaculated; #I's/E (E), number of intromissions preceding ejaculation for males that ejaculated; IR (E), intromission ratio for males that ejaculated.

	Vehicle	*20 μg trans-flu*	*10 μg cis-flu*	*15 μg cis-flu*	*20 μg cis-flu*
#E's (All)	2.50	2.00	1.88	1.50**	1.69*
# E's (E)	2.67 ± 0.13	2.46 ± 0.18	2.30 ± 0.13	2.00 ± 0.24	2.25 ± 0.21
# Males E	15	13	13	12	12
EL (All)	458.6 ± 97.7	771.4 ± 138.0	720.1 ± 146.0	945.4 ± 153.7**	865.5 ± 162.2*
EL (E)	367.2 ± 45.3	525.2 ± 62.7	481.3 ± 72.6	642.1 ± 99.7	595.3 ± 101.5
III (E)	33.1 ± 2.7	45.2 ± 5.2	46.5 ± 6.4	53.6 ± 7.4	54.6 ± 10.6
#I's/E (E)	11.1 ± 0.9	11.3 ± 0.8	10.0 ± 0.7	11.0 ± 0.9	10.7 ± 0.7
IR (E)	70.4 ± 4.3	71.5 ± 4.1	62.5 ± 4.6	66.9 ± 4.1	63.5 ± 2.6

$^{**}P < 0.01$, $^{*}P < 0.05$.

male was in the opposite goal box, and the remaining goal boxes were empty.

In preoperative conditioning the male received training trials every 3 days until he chose the goal box containing the female on at least 70% of the trials on which he made a choice. The rationale for calculating percent choice of the female based only on trials in which the male ran in the maze was to ensure separation of locomotor and motivational factors. At the beginning of each conditioning or test day the male was placed in the female's compartment until he achieved an initial intromission; all males did achieve an initial intromission. He was then placed into the center of the maze, and subsequent choices were recorded. The direction in which the male was faced when placed into the center of the maze was alternated. Tests were terminated after the male ejaculated or after 25 trials if the male failed to ejaculate. During preoperative conditioning the trials were not timed; otherwise, conditioning and test trials were conducted similarly.

Following implantation of a guide cannula into the MPOA, each male was given 3 postoperative tests over a period of two weeks, or until he again chose the females's goal box on at least 70% of those trials on which he made a choice. Three days later, all animals received a microinjection of either 20 μg cis-flupenthixol or vehicle, and were tested 5 min later. After 3 days they received the other treatment and were retested.

After the microinjection, the male was placed into the center of the maze and his latency to run to any arm of the maze was recorded. If an animal failed to move from the center of the maze within one minute, he was picked up and placed back down into the center of the maze to start a new trial. If he chose the female's goal box, he was allowed one intromission before starting a new trial; mounts were also recorded. If he chose any other arm of the maze, he was given 30 s to remain in the box before starting a new trial.

The following measures were recorded: the number of trials on which the male chose each goal box, the latency from the start of each trial until he crossed one of the black lines adjacent to a goal box, the number of trials in which the male failed to reach any goal box within 60 s, the number of trials on which he chose the female's goal box but failed to intromit, and the intromission ratio [100 × intromissions/(mounts + intromissions)] for those trials on which the male copulated with the female.

Data analysis

Experiments employed fully counterbalanced, repeated measures designs. Data were analyzed by repeated measures ANOVA, followed by Duncan's post hoc comparisons where appropriate. X-maze data were analyzed using repeated measures *t*-tests for vehicle vs drug.

Histology

Following each experiment, males were anesthetized and decapitated, after which their brains were removed and frozen in an American Optical cryostat. Forty-μm sections were cut, mounted on slides, stained with cresyl violet, and examined with a projection magnifier. Only those animals with histologically verifiable cannulae in the MPOA were included in data analysis.

RESULTS

Experiment 1. Effects on copulation of 10, 15 and 20 μg cis-flupenthixol, or 20 μg trans-flupenthixol in the MPOA

Following histology, data from 16 males were subjected to statistical analysis. Both the 15 μg and 20 μg doses of cis-flupenthixol significantly reduced the number of ejaculations during a 30 min test ($F_{4,60} = 2.57$, $P < 0.05$; see Fig. 1). This decrease resulted from nonsignificant reductions in both the number of animals that ejaculated and the number of ejaculations among those animals that did ejaculate (see Table I). The ejaculation

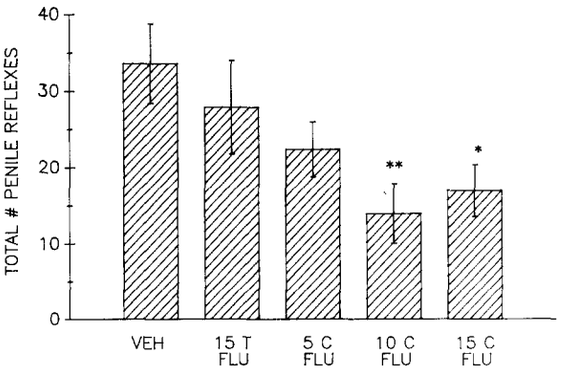

Fig. 2. Total number of penile reflexes per 30 min test following microinjection of vehicle (VEH), 15 μg/μl trans-flupenthixol (T FLU), 5, 10 or 15 μg/μl cis-flupenthixol (C FLU). Values are means ± standard errors. ($^{*}P < 0.05$, $^{**}P < 0.01$).

TABLE II

Effects of cis-flupenthixol microinjected into the MPOA on rat genital responses, Expt. 2

Values are means ± S.E.M. for RT, total number of penile reflexes; ET, total number of erections; E1, number of E1 erections; E2, number of E2 erections; E3, number of E3 erections; FT, total number of penile movements (flips); and CT, total number of reflex clusters.

	Vehicle	*15 μg trans-flu*	*5 μg cis-flu*	*10 μg cis-flu*	*15 μg cis-flu*
RT	33.59 ± 5.18	27.88 ± 6.11	22.35 ± 4.38	13.94 ± 4.15**	16.94 ± 3.90*
ET	27.76 ± 4.08	22.94 ± 4.68	19.06 ± 3.62	12.65 ± 3.88*	14.59 ± 3.39*
E1	11.47 ± 1.84	8.88 ± 2.13	8.88 ± 2.01	7.35 ± 2.42	6.71 ± 2.03
E2	14.00 ± 2.80	10.18 ± 2.52	8.82 ± 2.03	4.82 ± 1.96**	5.29 ± 1.31**
E3	2.29 ± 1.02	3.88 ± 1.25	1.29 ± 0.60	0.53 ± 0.26*	2.76 ± 0.87
FT	5.94 ± 1.72	4.94 ± 1.96	3.29 ± 1.10	1.29 ± 0.52**	2.35 ± 0.74*
CT	8.82 ± 1.24	7.29 ± 1.32	6.35 ± 1.07	4.65 ± 1.05**	4.29 ± 1.19**

$^{**}P < 0.01$, $^{*}P < 0.05$.

latency was significantly lengthened by the 15 and 20 μg doses of cis-flupenthixol only when maximum latencies were assigned to those animals that failed to ejaculate ($F_{4,60} = 2.66$, $P < 0.05$; see Table I). There was a nonsignificant trend toward an increase in interintromission interval by cis-flupenthixol among those animals that ejaculated ($0.05 < P < 0.1$). Trans-flupenthixol did not differ significantly from vehicle for any of the behavioral measures recorded.

Experiment 2. Effects on penile reflexes of 0, 5, 10, or 15 μg cis-flupenthixol, or 15 μg of trans-flupenthixol in the MPOA

Following histology, data from 17 males were subjected to statistical analysis. The 10 and 15 μg doses of cis-flupenthixol significantly decreased the total number of penile reflexes displayed ($F_{4,64} = 3.23$, $P < 0.025$; see Fig. 2). Reductions in both total erections and penile movements accounted for this decrease ($F_{4,64} = 2.78$, $P < 0.05$, and $F_{4,64} = 2.98$, $P < 0.05$, respectively; see Table II). The significance of the effect of cis-flupenthixol on erections was due predominantly to a decrease in the number of moderate (E2) erections ($F_{4,64} = 3.8$, $P < 0.01$). A significant decrease in the total number of reflex clusters was also noted ($F_{4,64} = 3.49$, $P < 0.025$). Trans-flupenthixol had no effect on any measure.

Experiment 3. Effects on locomotion and/or motivation of 0 or 20 μg cis-flupenthixol in the MPOA

Following histology, data from 17 males were subjected to statistical analysis. The 20 μg dose of cis-flupenthixol significantly reduced both the intromission ratio ($t_{16} = 2.40$, $P < 0.05$) and the percentage of trials on which the male chose the female's goal box ($t_{16} = 2.18$, $P < 0.05$; see Fig. 3). However, there were no statistically significant effects on the latency to reach the female's goal box, the latency to reach the other goal boxes, the percentage of trials on which the goal box containing the other male was chosen, or the number of trials on which the male did not move from the center of the maze (see Table III). In order to assess a potential relationship between cis-flupenthixol's effects on sexual motivation and on intromission ratio, the correlation coefficient for the difference between vehicle and cis-flupenthixol scores was calculated for percent choices of female and intromission ratio. The value ($r_{15} = 0.334$) was positive but not statistically significant.

DISCUSSION

In the present experiments cis-flupenthixol impaired copulatory behavior and decreased ex copula penile reflexes and sexual motivation. The decreased copulatory behavior observed in Expt. 1 replicates our previous findings[27], and shows inhibitory effects of a more moderate dose (15 μg). Furthermore, cis-flupenthixol's effect appears to be receptor mediated, since a high dose of the inactive isomer trans-flupenthixol produced no significant

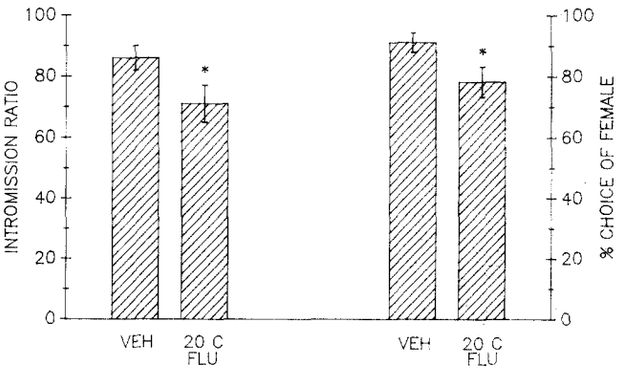

Fig. 3. Intromission ratio [100 × intromissions/(mounts ± intromissions)] and percent of trials in which male chose arm of maze containing female as opposed to other arms following microinjection of vehicle (VEH) or 20 μg/μl of cis-flupenthixol (C FLU). Values are means ± standard errors. ($^{*}P < 0.05$).

TABLE III

Effects of vehicle or cis-flupenthixol microinjections into the MPOA on X-maze behavior, Expt. 3

Values are means ± S.E.M. for IR, intromission ratio [100 × intromissons/(mount + intromissions)]; % Choice Female, percent of trials male chose female; Lat. Female, latency to goal box containing female; Lat. Other, latency to other goal boxes; # Trials w/o Move., number of trials male did not leave start area.

	IR	*% Choice Female*	*Lat. Female*	*Lat. Other*	*# Trials w/o Move*
Vehicle	86 ± 4	91.10 ± 3.23	10.07 ± 1.69	10.68 ± 3.14	1.22 ± 0.72
20 μg cis	71 ± 6*	78.20 ± 4.97*	13.51 ± 1.75	17.33 ± 4.09	0.83 ± 0.40

*$P < 0.05$.

changes in male copulatory behavior.

Previously we have reported a facilitation of both copulation[18] and penile reflexes[26] after microinjections of the dopamine agonist apomorphine into the MPOA. We now report that blocking endogenous dopamine stimulation in the MPOA, with cis-flupenthixol, impairs both copulation and penile reflexes. Erections and penile movements are thought to contribute to the male's ability to achieve a vaginal intromission[31], and both were decreased by cis-flupenthixol in the MPOA. Thus, at least one means by which cis-flupenthixol impairs copulation may be through inhibition of penile reflexes. Furthermore, the effectiveness of a lower dose (10 μg) in the reflex tests suggests that penile reflexes are more susceptible to disruption by dopamine antagonists in the MPOA than is copulation.

In order to test whether locomotor or motivational deficits may also have contributed to the impairments in copulation, animals were tested in the X-maze following injections of 20 μg cis-flupenthixol or vehicle. While locomotor activity was not significantly affected by cis-flupenthixol, males did show a decrease in sexual motivation, as evidenced by a reduction in the number of trials on which the male chose the goal box containing a receptive female. In addition, the intromission ratio (a measure of the success of attempted intromissions) was impaired by cis-flupenthixol. Since erections and penile movements contribute to the successful performance of intromission, the decrease in intromission ratio may have reflected an impairment in erectile ability. The lack of a significant reduction in intromission ratio in Expt. 1 may have resulted from a lower value on vehicle tests in that experiment. In Expt. 1, the intromission ratio was reduced from 71 to an average of 64 by cis-flupenthixol; in Expt. 3, the values were 86 and 71, respectively. The animals in Expt. 3 had had considerably more sexual experience before drug trials began.

The reductions in both penile responses and sexual motivation in these experiments suggest either that endogenous dopamine activity in the MPOA contributes to both reflexive and motivational components of sexual behavior, or that it influences primarily genital responses, which in turn influences motivation. In order to test this hypothesis indirectly, we calculated the correlation coefficient between the effects of cis-flupenthixol on percent choice of the female and on intromission ratio in Expt. 3, assuming that the intromission ratio at least partially reflects genital response function. The correlation coefficient was positive ($r_{15} = 0.334$) but not statistically significant, suggesting that mechanisms controlling reflexes may contribute to sexual motivation, but that other factors may be more important.

The pattern of results observed in these experiments is especially interesting when contrasted with the effects of apomorphine microinjections into the ventral tegmental area (VTA), the source of the mesocorticolimbic dopamine tract. Such treatments stimulate the impulse regulating autoreceptors on dopamine cell bodies and dendrites in the VTA and thereby decrease the rate of firing of these neurons[1,35]. As in the present experiments, the presumed slowing of the activity of the mesocorticolimbic dopamine tract slowed copulation and resulted in fewer ejaculations[17]. In contrast to the present experiments, this treatment did not affect ex copula genital reflexes or percent choice of the female in an X-maze[19]. However, it slowed the rate of running to all arms of the X-maze, increased the number of trials on which the male failed to move from the center of the X-maze, and increased the number of misdirected mount attempts in videotaped copulation tests. Thus, manipulation of the mesocorticolimbic dopamine tract preferentially altered locomotor and/or motor planning and execution factors in copulation, whereas manipulation of incertohypothalamic synapses in the MPOA preferentially affected the reflexive and motivational components of copulation.

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REFERENCES

1 Aghajanian, G.K. and Bunny, B.S., Dopamine 'autoreceptors'. Pharmacological characterization by microiontophoretic single cell recording studies, *Naunyn Schmiedebergs Arch. Pharmacol.*, 297 (1977) 1–7.

2 Ahlenius, S. and Larsson, K., Apomorphine and haloperidol-induced effects on male rat sexual behavior: no evidence for actions due to stimulation of central dopamine autoreceptors, *Physiol. Biochem. Behav.*, 21 (1984) 463–466.

3 Baggio, G. and Ferrari, F., The role of dopaminergic receptors in the behavioral effects induced by lisuride in male rats, *Psychopharmacology*, 80 (1983) 38–42.

4 Barbeau, A., L-DOPA therapy in Parkinson's disease, a critical review of nine years experience, *Can. Med. Assoc. J.*, 101 (1969) 791–800.

5 Baum, M.J. and Starr, M.S., Inhibition of sexual behavior by dopamine antagonists or serotonin agonist drugs in castrated male rats given estradiol or dihydrotestosterone, *Pharmacol. Biochem. Behav.*, 13 (1980) 57–67.

6 Benassi-Benelli, A., Ferrari, F. and Quarantotti, B., Penile erection induced by apomorphine and *N-n*-propyl-norapomorphine in rats, *Arch. Int. Pharmacodyn. Ther.*, 242 (1979) 241–247.

7 Björklund, A., Lindvall, O. and Nobin, A., Evidence of an incertohypothalamic dopamine neurone system in the rat, *Brain Research*, 89 (1975) 29–42.

8 Bowers, M.B., Van Woert, M. and Davis, L., Sexual behavior during L-DOPA treatment for Parkinsonism, *Am. J. Psychiat.*, 127 (1971) 1691.

9 Clark, J.T., Stefanick, M.L., Smith, E.R. and Davidson, J.M., Further studies on alterations in male rat copulatory behavior induced by the dopamine-receptor agonist RDS-127, *Pharmacol. Biochem. Behav.*, 19 (1983) 781–786.

10 Foreman, M.M. and Hall, J.L., Effects of D2-dopaminergic receptor stimulation on male rat sexual behavior, *J. Neural Transm.*, 68 (1987) 153–170.

11 Giantonio, G.W., Lund, N.L. and Gerall, A.A., Effects of diencephalic and rhinencephalic lesions on the male rat's sexual behavior, *J. Comp. Physiol. Psychol.*, 73 (1970) 38–46.

12 Gower, A.J., Berendsen, H.H.G., Princen, M.M. and Broekkamp, C.L.E., The yawning-penile erection syndrome as a model for putative dopamine autoreceptor activity, *Eur. J. Pharmacol.*, 103 (1984) 81–89.

13 Gray, G.D., Davis, H.N. and Dewsbury, D.A., Effects of L-DOPA on the heterosexual behavior of male rats, *Eur. J. Pharmacol.*, 27 (1975) 367–370.

14 Hart, B.L., Sexual reflexes and mating behavior in the male rat, *J. Comp. Physiol. Psychol.*, 65 (1968) 453–460.

15 Heimer, L. and Larsson, K., Impairment of mating behavior in male rats following lesions in the preoptic-anterior hypothalamic continuum, *Brain Research*, 3 (1966/1967) 248–263.

16 Holmes, G.M., Holmes, D.G. and Sachs, B.D., An IBM-PC based data collection system for recording rodent sexual behavior and for general event recording, *Physiol. Behav.*, 44 (1988) 825–828.

17 Hull, E.M., Bazzett, T.J., Warner, R.K., Eaton, R.C. and Thompson, J.T., Dopamine receptors in the ventral tegmental area modulate male sexual behavior in rats, *Brain Research*, 512 (1990) 1–6.

18 Hull, E.M., Bitran, D., Pehek, E.A., Warner, R.K., Band, L.C. and Holmes, G.M., Dopaminergic control of male sexual behavior in rats: effects of an intracerebrally-infused agonist. *Brain Research*, 370 (1986) 73–81.

19 Hull, E.M., Weber, M.S., Eaton, R.C., Dua, R., Markowski, V.P., Lumley, L.A. and Moses, J., Dopamine receptors in the ventral tegmental area affect motor, but not motivational or reflexive, components of copulation in male rats, submitted.

20 Malmnas, C.O., Monoaminergic influence on testosterone-activated copulatory behavior in the castrated male rat, *Acta Physiol. Scand., Suppl.*, 395 (1973) 1–128.

21 Malmnas, C.O., Dopaminergic reversal of the decline after castration of rat copulatory behavior, *J. Endocrinol.*, 73 (1977) 187–188.

22 Malsbury, C.W. and Pfaff, D.W., Neural and hormonal determinants of mating behavior in adult male rats. In L. DiCara (Ed.), *The Limbic and Autonomic Nervous Systems: Advances in Research*, Plenum, New York, 1974, pp. 86–136.

23 Merari, A. and Ginton, A., Characteristics of exaggerated sexual behavior induced by electrical stimulation of the medial preoptic area in male rats, *Brain Research*, 86 (1975) 97–108.

24 Napoli-Farris, L., Fratta, W. and Gessa, G.L., Stimulation of dopamine autoreceptors elicits 'premature ejaculation' in rats, *Pharmacol. Biochem. Behav.*, 20 (1984) 69–72.

25 Pehek, E.A., Thompson, J.T., Eaton, R.C., Bazzett, T.J. and Hull, E.M., Apomorphine and haloperidol, but not domperidone, affect penile reflexes in rats, *Pharmacol. Biochem. Behav.*, 31 (1988) 201–208.

26 Pehek, E.A., Thompson, J.T. and Hull, E.M., The effects of intrathecal administration of the dopamine agonist apomorphine on penile reflexes and copulation in the rat, *Psychopharmacology*, 99 (1989) 304–308.

27 Pehek, E.A., Warner, R.K., Bazzett, T.J., Bitran, D., Band, L.C., Eaton, R.C. and Hull, E.M., Microinjections of cis-flupenthixol, a dopamine antagonist, into the medial preoptic area impairs sexual behavior of male rats, *Brain Research*, 443 (1988) 70–76.

28 Pellegrino, L.J., Pellegrino, A.S. and Cushman, A.J., A *Stereotaxic Atlas of the Rat Brain*, 2nd edn., Plenum, New York, 1979.

29 Pierini, A.A. and Nusimovich, B., Male diabetic impotence: effects of dopaminergic agents, *Arch. Androl.*, 6 (1981) 347–350.

30 Tagliamonte, A., Fratta, W., Del Fiacco, M. and Gessa, G.L., Possible stimulatory role of brain dopamine in the copulatory behavior of male rats, *Pharmacol. Biochem. Behav.*, 2 (1974) 257–260.

31 Sachs, B.D., Potency and fertility: hormonal and mechanical causes and effects of penile actions in rats. In J. Balthazart, E. Prove and R. Gilles (Eds.), *Hormones and Behavior in Higher Vertebrates*, Springer, Berlin, 1983, pp. 86–110.

32 Sachs, B.D. and Meisel, R.L., The physiology of male sexual behavior. In E. Knobil and J. Neill (Eds.), *The Physiology of Reproduction, Vol. 2*, Raven, New York, 1988, pp. 1393–1485.

33 Serra, G., Collu, M., Loddo, A., Celasco, G. and Gessa, G.L., Hypophysectomy prevents yawning and penile erections but not hypomotility induced by apomorphine, *Pharmacol. Biochem. Behav.*, 19 (1983) 917–919.

34 Vogel, H.P. and Schiffter, R., Hypersexuality — a complication of dopaminergic therapy in Parkinson's disease, *Pharmacopsychiatry*, 16 (1983) 107–110.

35 White, F.J. and Wang, R.Y., Pharmacological characterization of dopamine autoreceptors in the rat ventral tegmental area: microiontophoretic studies, *J. Pharmacol. Exp. Ther.*, 195 (1984) 275–280.