Pharmacology Biochemistry & Behavior, Vol. 35, pp. 327–334. © Pergamon Press plc, 1990. Printed in the U.S.A. 0091-3057/90 $3.00 + .00

Catecholamines and the Initiation of Sexual Behavior in Male Rats Without Sexual Experience

ANDERS ÅGMO[1] AND ZIVA PICKER

Department of Psychology, Universidad Anáhuac, Mexico City

Received 2 March 1989

ÅGMO, A. AND Z. PICKER. *Catecholamines and the initiation of sexual behavior in male rats without sexual experience.* PHARMACOL BIOCHEM BEHAV **35**(2) 327–334, 1990.—The purpose of the present experiments was to investigate the effects of modified catecholaminergic neurotransmission upon sexual behavior in inexperienced males. Such males are critically dependent on stimuli from the female in order to initiate sexual behavior, and catecholamines are known to modulate interactions with environmental stimuli. It was found that D-amphetamine, 0.5 and 1 mg/kg, and amfonelic acid, 0.25 and 0.5 mg/kg, reduced mount and intromission latencies. Pimozide, in doses between 0.25 and 1 mg/kg, and cis(Z)-flupentixol, 0.5 mg/kg, reduced the proportion of animals displaying sexual behavior. The noradrenergic neurotoxin DSP4 (50 mg/kg one week before behavioral observation) shortened intromission latency while the noradrenaline precursor threo-dihydroxyphenylserine (10 mg/kg + carbidopa 50 mg/kg) increased mount and intromission latencies. In a test for social and exploratory behaviors it was found that amfonelic acid, in a dose of 0.5 mg/kg, augmented sniffing and rearing without affecting nonsexual interaction with a receptive female. Flupentixol (0.5 mg/kg) had a slight inhibitory effect on exploratory behavior and no effect on nonsexual interaction with a female. It is suggested that enhanced dopaminergic activity facilitates the initiation of sexual behavior due to an increased general arousal and not because of a specific effect on that behavior. The role of noradrenaline is less clear at present.

Sexual behavior Dopamine Noradrenaline Male rat

THE role of dopamine in the control of male sexual behavior is far from clear. Although several authors have proposed a facilitatory effect [reviewed in (10)], many data do not coincide with such a hypothesis [for a critical discussion see (1)]. We have suggested that dopamine becomes of importance only in situations where the male's sexual behavior is critically dependent on environmental stimuli (1). In such situations, increased dopaminergic neurotransmission would, according to our hypothesis, facilitate initiation of sexual behavior without affecting its execution. The data supporting this hypothesis were obtained in a study where it was found that increased dopaminergic activity failed to affect sexual behavior in expert copulators, while mount latencies were reduced in castrated males made to display a low level of sexual activity with weekly injections of testosterone propionate.

Intact, experienced males require only limited sensory stimulation in order to initiate sexual behavior. This is illustrated in short mount latencies, and a lack of correlation between female proceptivity and intensity of male sexual behavior (19). In castrated animals given small doses of testosterone, mount latencies are longer and female proceptivity critical for initiation of sexual behavior [Ågmo, unpublished; (21,22)]. This kind of animal, thus, seems to require a larger amount of environmental stimulation in order to display copulatory behavior.

Dopamine has been proposed to increase the animal's arousal level (46), to make more efficient the processing of sensory information (32), or to participate in attentional mechanisms (12). All these actions could easily explain the effects of dopamine on sexual behavior, and there would be no need to suppose an action on mechanisms specifically involved in the control of that behavior.

The first purpose of the present studies was to further investigate the above mentioned hypothesis, using male rats without sexual experience. Such animals are critically dependent on stimuli from the female in order to initiate copulatory behavior (33), and are particularly sensitive to destruction of sensory modalities [reviewed in (30)]. It was predicted that increased dopaminergic activity would reduce mount latencies, and that dopamine antagonists would prolong them without having effects on sexual behavior once initiated. In an additional experiment, the effects of manipulations of dopaminergic neurotransmission on exloratory behavior and social interaction were evaluated. If dopamine indeed influences interaction with environmental stimuli, exploratory behaviors should be modified more or as much as social behaviors.

Noradrenaline has been suggested to have effects opposite to those of dopamine with regard to interaction with environmental

[1]Requests for reprints should be addressed to Anders Ågmo, Escuela de Psicología, Universidad Anáhuac, Apdo. Postal 10-844, 11000 México 10, D.F., Mexico.

TABLE 1

SEXUAL BEHAVIOR IN MALE RATS WITHOUT SEXUAL EXPERIENCE AFTER FACILITATED DOPAMINERGIC NEUROTRANSMISSION

Behavior Parameter	Vehicle	Amphetamine 0.25	Amphetamine 0.5	Amphetamine 1	Vehicle	Amfonelic 0.25	Amfonelic 0.5
Mount percentage	48	48	56	40	52	60	56
Intromission percentage	40	40	56	40	48	60	48
Ejaculation percentage	12	16	24	28	40	52	36
Mount latency	7.1 ± 1.3	5.5 ± 2.1	3.0 ± 0.8*	2.2 ± 0.3†	5.0 ± 0.9	3.0 ± 0.7*	2.9 ± 0.5*
Intromission latency	9.1 ± 1.8	4.5 ± 2.6	4.1 ± 0.9*	3.4 ± 0.7†	6.0 ± 0.8	2.9 ± 0.8*	2.8 ± 0.4†
Ejaculation latency	21.2 ± 2.4	19.4 ± 4.2	14.8 ± 2.0	21.3 ± 4.4	14.3 ± 2.7	9.4 ± 2.0	18.4 ± 2.5
Postejaculatory interval	9.3 ± 0.7	8.6 ± 0.9	10.2 ± 1.0	7.9 ± 0.8	7.2 ± 0.6	7.1 ± 0.2	8.3 ± 0.4
Number of mounts	23.7 ± 7.5	13.3 ± 6.8	9.9 ± 1.0	18.6 ± 7.2	13.0 ± 3.7	8.6 ± 2.1	16.2 ± 1.7
Number of intromissions	12.7 ± 1.2	10.0 ± 2.1	13.4 ± 1.5	15.3 ± 2.1	9.1 ± 1.0	10.6 ± 0.7	18.9 ± 2.3*

*Different from vehicle, $p<0.05$, †$p<0.01$.
Data are means ± SE. Latencies in min. Doses in mg/kg. N = 25 per group.

stimuli [reviewed in (36)]. Its effects on sexual behavior are less clear. Most recent studies have employed agonists or antagonists for specific adrenergic receptors. For example, stimulation of α_1 receptors as well as blockade of α_2 receptors has been proposed to be stimulatory (13). In case that α_2 receptors always were presynaptic and α_1 receptors always postsynaptic, this would imply a facilitatory role of noradrenaline in the control of sexual behavior. However, recent data suggest that such a clear-cut location of α_1 and α_2 receptors is overly simplified (48). Moreover, both the noradrenaline synthesis inhibitor FLA 63, and the receptor antagonists phenoxybenzamine and propranolol have been reported to be without effect (34). The noradrenaline precursor threo-dihydroxyphenylserine has been found to have a slight inhibitory effect (34), while depletion of noradrenaline in the dorsal bundle with the neurotoxin DSP4 has been reported to slightly increase the postejaculatory interval (20). It is not possible, therefore, to make definite predictions as to the effects of increased or decreased noradrenergic transmission on sexual behavior. Nevertheless, if the effects upon interaction with environmental stimuli are of importance, depletion of noradrenaline would facilitate initiation of sexual behavior without affecting subsequent sexual activity in animals without sexual experience, and increase of noradrenergic activity would inhibit initiation of sexual behavior. The evaluation of this hypothesis was the last purpose of the present studies.

METHOD

Subjects

Four hundred and seventy-four male Wistar rats (300–400 g) from a local colony were used. They were housed two per cage under a reversed light/dark cycle (12/12 hr) at constant temperature (22°C) and given commercial rat pellets and water ad lib. All males had been separated from female littermates at weaning, and had since remained without access to females until the present experiment. It must be noted, though, that they were housed in the same room as the females until about three weeks before the experiment.

Females (Wistar, 200–300 g) used in the mating tests were ovariectomized under Brevital anesthesia (40 mg/kg) at least two weeks before use and subcutaneously injected with 25 μg of estradiol benzoate (Sigma) 52–56 hr before use and with 1 mg/rat of progesterone (Aldrich) 4–8 hr before. The steroids were dissolved in corn oil and injected in a volume of 0.2 ml/rat.

Behavioral Testing Procedure

In tests for sexual behavior, the male was introduced into the observation cage (40 × 60 × 40 cm) where a female had already been placed. Care was taken to use only females displaying proceptive behaviors, such as darting, hopping and ear wiggling. The following parameters of sexual behavior were recorded: mount latency, time from introduction of the male until the first mount with pelvic thrusting; intromission latency, time from introduction of the male until the first vaginal penetration; ejaculation latency, time from the first intromission until ejaculation; postejaculatory interval, time from ejaculation until the next intromission; the number of preejaculatory mounts and intromissions. The test was ended when one of the following criteria was met: mount or intromission latency longer than 15 min, ejaculation latency longer than 30 min, end of the first postejaculatory interval.

Tests for exploratory behaviors and social interaction lasted 10 min after introduction of the male in the observation cage where a female had already been placed. The observed behaviors were

TABLE 2

SEXUAL BEHAVIOR IN MALE RATS WITHOUT SEXUAL EXPERIENCE AFTER IMPAIRED DOPAMINERGIC NEUROTRANSMISSION

Behavior Parameter	Vehicle	Pimozide 0.25	Pimozide 0.5	Pimozide 1	Vehicle	Flupentixol 0.25	Flupentixol 0.5
Mount percentage	61	24*	24*	0‡	52	32	20*
Intromission percentage	50	20*	21	0†	48	28	16*
Ejaculation percentage	22	20	21	0	48	24	16*
Mount latency	3.0 ± 0.5	3.8 ± 0.8	4.2 ± 0.6	—	3.7 ± 0.7	4.8 ± 1.5	2.1 ± 0.3
Intromission latency	4.6 ± 1.1	5.1 ± 0.7	4.4 ± 0.6	—	4.3 ± 0.6	6.1 ± 1.7	4.4 ± 1.7
Ejaculation latency	14.4 ± 2.3	17.3 ± 2.3	15.1 ± 1.9	—	13.5 ± 1.7	11.9 ± 2.1	11.5 ± 1.3
Postejaculatory interval	10.1 ± 1.8	8.3 ± 0.8	11.8 ± 1.0	—	7.2 ± 0.4	7.6 ± 0.5	7.6 ± 0.5
Number of mounts	21.3 ± 4.5	20.0 ± 5.5	9.6 ± 1.9*	—	8.8 ± 1.2	14.8 ± 2.6	8.5 ± 2.5
Number of intromissions	17.0 ± 3.5	14.4 ± 2.5	11.4 ± 1.4	—	9.4 ± 1.2	7.7 ± 2.0	7.0 ± 1.2

*Different from control, $p<0.05$, †$p<0.01$, ‡$p<0.001$.

Data are means ± SE. Latencies in min. Doses in mg/kg. N=25 (flupentixol all doses, pimozide 0.25 mg/kg), 33 (pimozide 0.5 kg/kg) and 18 (pimozide vehicle and pimozide 1 mg/kg).

classified according to Meyerson and Hoglund (37), as modified by Paredes and Ågmo (41). The behavioral categories were the following: rearing, standing on the hindlegs; sniffing, rapid movements of the head and whiskers while the animal explores; resting, lying or standing still without any particular overt behavior; self-grooming, licking or gently biting different areas of the fur, of the limbs, or of the genital area as well as movements of any limb directed to any part of the body; grooming partner, licking or gently biting any area of the partner, except the genital area; genital exploration, sniffing or licking the partner's anogenital region; pursuit, the experimental animal follows the partner keeping close contact. These behaviors were recorded on a keyboard connected to an electronic equipment located in an adjacent room. This equipment registered the frequency and duration of each behavior. The tests for exploratory and social behavior were performed in additional groups of animals, independent from observations on sexual behavior.

Drugs

In order to increase dopaminergic neurotransmission, D-amphetamine sulphate (Sigma) and amfonelic acid (Sterling-Winthrop) were used. Amphetamine was dissolved in distilled water and amfonelic acid in 0.5 ml hot 0.1 M NaOH, and then diluted in saline to the appropriate concentration. Amphetamine appears to release mainly newly synthetized dopamine (29), and, in addition, either facilitate or inhibit noradrenergic transmission, depending on brain structure (15,19). Amfonelic acid releases mainly vesicular dopamine, and has slight actions on noradrenergic neurons (38,44). Thus, these drugs have different actions but produce one common end result, increased levels of synaptic dopamine. Therefore, any common behavioral effect should be due to this common end result.

Reduced dopaminergic neurotransmission was achieved using the receptor antagonists pimozide (Janssen de Mexico) and cis(Z)-flupentixol (Lundbeck). Pimozide was dissolved in a few drops of glacial acetic acid, diluted with hot saline to the appropriate concentration, and the pH adjusted to about 5 with 1 M NaOH. Flupentixol was dissolved in distilled water. Pimozide preferentially blocks the D_2 receptor, and flupentixol has about the same affinity for both the D_1 and the D_2 receptor (24).

Facilitated noradrenergic transmission was achieved by the administration of the peripheral inhibitor of aromatic amino acid decarboxylase, carbidopa (Merck Sharp and Dohme) plus the specific noradrenaline precursor DL-threo-dihydroxyphenylserine (DOPS; Sigma). Carbidopa was dissolved in hot distilled water to which 1 M HCl was added until a clear solution was obtained. DOPS was dissolved in hot distilled water. This procedure has been shown to reliably and specifically increase cerebral noradrenaline, provided that the dose of DOPS is not excessive (9).

In order to reduce noradrenergic transmission, the neurotoxin DSP4 (N-2-chloroethyl-N-ethyl-2-bromobenzylamine; Astra) was used. This neurotoxin destroys noradrenergic neurons throughout the body. However, after a few days, peripheral noradrenaline levels approach normal, whereas the depletion in the central nervous system seems to be permanent (25,26).

All drugs were administered intraperitoneally, in a volume of 1 ml/kg b.wt. (amphetamine and flupentixol) or 5 ml/kg b.wt. (all other drugs). The intervals between drug injection and behavioral observation were the following: amfonelic acid, 15 min; flupentixol and DOPS, 30 min; amphetamine, 40 min; carbidopa and

TABLE 3

SEXUAL BEHAVIOR IN MALE RATS WITHOUT SEXUAL EXPERIENCE AFTER IMPAIRED OR FACILITATED NORADRENERGIC NEUROTRANSMISSION

Behavior Parameter	Vehicle	DSP4 50	Vehicle[a]	DOPS 10[a]
Mount percentage	44	36	36	28
Intromission percentage	44	36	28	16
Ejaculation percentage	36	36	20	12
Mount latency	7.3 ± 1.2	4.4 ± 1.2	4.1 ± 1.8	8.1 ± 1.1*
Intromission latency	7.5 ± 1.2	3.6 ± 0.9*	3.2 ± 0.6	8.4 ± 1.4†
Ejaculation latency	12.5 ± 2.4	11.6 ± 1.5	13.5 ± 2.4	8.9 ± 3.6
Postejaculatory interval	6.4 ± 0.4	7.9 ± 0.8	7.2 ± 0.3	9.4 ± 0.8*
Number of mounts	9.1 ± 2.7	6.8 ± 2.1	7.0 ± 2.2	3.7 ± 1.2
Number of intromissions	10.6 ± 1.2	10.6 ± 1.5	12.2 ± 0.9	7.7 ± 0.3†

*Different from control, $p<0.05$, †$p<0.01$.
[a]+carbidopa, 50 mg/kg.
Data are means ± SE. Latencies in min. Doses in mg/kg. N = 25 per group.

pimozide, 60 min; DSP4, 1 week.

A parallel groups design was used in such a way that for each drug, all the doses employed and the appropriate vehicle were administered to an equal number of animals at each session. No animal was used more than once.

Statistical Analysis

The proportion of animals displaying mounts, intromissions and ejaculation was evaluated with the χ^2 test. Whenever a significant difference was obtained, all drug-treated groups were compared with vehicle using additional χ^2 tests. In the latter case, whenever the expected frequency was less than 5 in any cell, the Fisher exact probability test was used. Analyses of the mount, intromission and ejaculation latencies, as well as of the postejaculatory interval, were performed using data only from animals displaying sexual activity. This was considered more adequate than assigning latencies to animals that did not display sexual behavior. These parameters were evaluated with ANOVA followed by the Tukey LSD procedure in case of significance. The number of mounts and intromissions was analyzed only for animals that ejaculated, using ANOVA followed by the Tukey test. In that way, the number of mounts and intromissions required for ejaculation was evaluated rather than total number of mounts and intromissions displayed. In case that only one dose of a drug was used, it was compared to control with the *t*-test.

Frequency and total duration of exploratory behavior and social interaction were analyzed with a one-factor MANOVA. In case of significant omnibus test, univariate ANOVA was performed for each parameter, and the Bonferroni correction applied to protect significance levels. The mean duration of each occurrence of the exploratory and social behaviors was evaluated with univariate ANOVAs. The fact that the number of animals actually displaying these behaviors were different in different treatments excluded the use of MANOVA. Obviously, the mean duration of a behavior could not be calculated if it did not occur. Also here, the Bonferroni correction was used. A posteriori comparisons were performed with the Tukey procedure.

RESULTS

As can be seen in Table 1, both amphetamine and amfonelic acid reduced mount and intromission latencies. Amphetamine had no other effects on sexual behavior. Amfonelic acid, in a dose of 0.5 mg/kg, increased the number of preejaculatory intromissions. The proportion of animals displaying mounts, intromissions or ejaculation was not modified by these drugs.

The dopamine antagonists pimozide and flupentixol did not modify sexual behavior in the animals that copulated. However, the proportion of animals displaying mounts and intromissions was reduced by both drugs, and flupentixol also reduced the proportion of animals achieving ejaculation. The lack of a significant effect of pimozide on the latter behavior is due to the fact that only a small proportion of the animals treated with vehicle ejaculated. Indeed, after pimozide, 1 mg/kg, sexual behavior was abolished. Data are shown in Table 2.

The noradrenergic neurotoxin DSP4 reduced the intromission latency, without affecting other parameters of sexual behavior. The noradrenaline precursor, DOPS, prolonged the mount and intromission latencies. It also prolonged the postejaculatory inter-

TABLE 4

FREQUENCIES OF EXPLORATORY AND SOCIAL BEHAVIORS DURING A 10-MIN TEST IN MALE RATS WITHOUT SEXUAL EXPERIENCE TREATED WITH AMFONELIC ACID, 0.5 mg/kg, OR WITH FLUPENTIXOL, 0.5 mg/kg

Behavior Category	Vehicle	Amfonelic Acid	Flupentixol
Sniffing	18.2 ± 2.3	57.7 ± 7.3*	12.1 ± 2.2
Rearing	12.6 ± 2.0	42.7 ± 7.4*	8.9 ± 1.7
Resting	3.8 ± 1.4	4.0 ± 1.6	3.1 ± 0.9
Self-grooming	10.4 ± 2.1	12.0 ± 3.1	6.3 ± 1.5
Grooming partner	3.6 ± 0.9	8.4 ± 2.9	1.5 ± 0.6
Genital exploration	0.9 ± 0.6	0.3 ± 0.1	0
Pursuit	4.1 ± 2.2	5.9 ± 2.9	1.0 ± 0.9
Incomplete mounts	0.1 ± 0.1	1.0 ± 0.9	0

*Different from vehicle, $p<0.01$.
Data are means ± SE. N = 10 per group.

val and reduced the number of intromissions preceding ejaculation (Table 3).

When the frequency of exploratory and social behaviors was evaluated after treatment with amfonelic acid or flupentixol, a significant effect of treatment was obtained in the MANOVA [Pillai's V = 1.083, F(16,42) = 3.10, $p = 0.002$]. Univariate ANOVAs showed a significant effect on the frequency of sniffing and rearing, F(2,27) = 29.06, $p<0.001$, and, F(2,27) = 16.68, $p<0.001$, respectively. A posteriori Tukey tests showed that the frequency of sniffing and rearing was higher after treatment with amfonelic acid than after treatment with vehicle. Flupentixol had no effect (Table 4).

The total duration of exploratory and social behaviors was also modified by the drug treatment, as shown in the MANOVA [Pillai's V = 0.973, F(14,44) = 2.98, $p = 0.003$]. Univariate ANOVAs showed an effect only on duration of sniffing, F(2,27) = 10.18, $p = 0.001$. When the Tukey test was performed, it was found that the total duration of sniffing was shorter after treatment with flupentixol than after treatment with amfonelic acid, while neither drug was different from control (Table 5).

TABLE 5

TOTAL DURATION (IN SEC) OF EXPLORATORY AND SOCIAL BEHAVIORS DURING A 10-MIN TEST IN MALE RATS WITHOUT SEXUAL EXPERIENCE TREATED WITH AMFONELIC ACID, 0.5 mg/kg, OR WITH FLUPENTIXOL, 0.5 mg/kg

Behavior Category	Vehicle	Amfonelic Acid	Flupentixol
Sniffing	187.3 ± 35.6	266.7 ± 18.3	103.8 ± 18.8
Rearing	58.7 ± 12.0	120.4 ± 29.2	53.3 ± 12.6
Resting	143.1 ± 64.2	64.7 ± 28.0	305.5 ± 59.9
Self-grooming	157.4 ± 39.8	73.1 ± 23.1	133.8 ± 46.6
Grooming partner	24.6 ± 9.9	34.5 ± 10.8	7.7 ± 3.6
Genital exploration	5.4 ± 4.1	0.5 ± 0.3	0
Pursuit	18.6 ± 9.7	30.2 ± 14.4	4.0 ± 3.4

Data are means ± SE. N = 10 per group.

TABLE 6

DURATION (IN SEC) OF EACH OCCURRENCE OF EXPLORATORY AND SOCIAL BEHAVIORS IN A 10-MIN TEST IN MALE RATS WITHOUT SEXUAL EXPERIENCE TREATED WITH AMFONELIC ACID, 0.5 mg/kg, OR WITH FLUPENTIXOL, 0.5 mg/kg

Behavior Category	Vehicle	Amfonelic Acid	Flupentixol
Sniffing	9.9 ± 0.9	5.1 ± 0.6†	9.2 ± 0.9
Rearing	4.4 ± 0.4	2.6 ± 0.8†	6.0 ± 0.6*
Resting	38.2 ± 16.8	20.2 ± 11.1	176.8 ± 58.3
Self-grooming	13.7 ± 1.6	5.9 ± 0.7	19.2 ± 4.7
Grooming partner	5.8 ± 0.9	4.6 ± 0.7	4.7 ± 0.5
Genital exploration	5.7 ± 0.9	1.5 ± 0.5	—
Pursuit	4.6 ± 0.4	5.7 ± 0.8	4.8 ± 0.9

*Different from control, $p<0.05$, †$p<0.01$.
Data are means ± SE. N = 10 per group.

When the duration of each occurrence of the exploratory and social behaviors was analyzed with univariate ANOVAs, only the duration of each occurrence of sniffing and rearing was modified, F(2,27) = 9.49, $p = 0.0008$, and, F(2,27) = 15.25, $p<0.0001$, respectively. The Tukey test showed that the duration of each occurrence of sniffing was shorter after treatment with amfonelic acid than after treatment with vehicle. Flupentixol had no effect. The duration of each occurrence of rearing was shorter after amfonelic acid and longer after flupentixol than after vehicle (Table 6).

Taken together, these data show that amfonelic acid modifies exploratory behaviors (sniffing and rearing) and leave behaviors related to interaction with the female unaffected. Flupentixol has a slight effect on exploratory behavior (increasing the duration of each occurrence of rearing) and none at all on nonsexual behaviors related to the female.

DISCUSSION

The present data show that augmented dopaminergic neurotransmission facilitates the initiation of sexual behavior in male rats without sexual experience. In agreement with previous data (1), amphetamine and amfonelic acid did not consistently affect ejaculatory mechanisms. Indeed, the only effect observed upon parameters of ejaculatory behavior was an increased number of preejaculatory intromissions after amfonelic acid 0.5 mg/kg. The functional significance of this effect is difficult to evaluate, particularly since it was not obtained with amphetamine. It may even be a spurious effect. The lack of a role of dopamine in the control of ejaculatory mechanisms is further supported by the fact that the antagonists flupentixol and pimozide failed to modify parameters of sexual behavior once initiated.

It could be argued that since the mount and intromission latencies were reduced after treatment with amphetamine or amfonelic acid, the postejaculatory interval should also be reduced. These latencies, together with the postejaculatory interval, have been proposed to constitute a sexual arousal mechanism (8), and these parameters could, therefore, be expected to be similarly affected by drug treatments. This was not the case in the present studies. However, in a factor analytic study of components of male

sexual behavior, it was found that the postejaculatory interval did not load significantly on the same factor as mount and intromission latencies (43). It was suggested that "postejaculatory refractoriness may be under the control of processes different from those controlling initial sexual arousal" [(43), p. 274]. Present data support this hypothesis.

The absence of an effect upon ejaculatory mechanisms seen after treatment with amphetamine and amfonelic acid might appear to contradict earlier data obtained with dopamine agonists. For example, Butcher *et al.* (11) reported that apomorphine, in a dose with clear postsynaptic actions, reduced the number of preejaculatory intromissions, while amphetamine reduced ejaculation latency. Several other studies have confirmed facilitatory effects of apomorphine doses acting postsynaptically (2,47). However, conflicting data have been abundant. Low doses of apomorphine, mainly acting at autoreceptor sites, thereby reducing dopaminergic transmission, have also been found to reduce the number of preejaculatory intromissions and ejaculation latency (39, 40, 42). The dopamine autoreceptor agonist BHT-920 has similar effects (16,17). Amphetamine has been reported to be without effect on ejaculatory mechanisms (45), while dopamine receptor agonists such as quinpirole, pergolide or bromocriptine in postsynaptically active doses have been found to have effects similar to autoreceptor active doses of apomorphine (3,4). Interestingly, both apomorphine and the D_2 receptor agonist LY 163502 have been found to inhibit sexual behavior in doses acting at the autoreceptor (18,23). Studies with dopamine antagonists are equally confusing [discussed in (1)].

To make any sense out of these contradictory data is not easy. The only reasonable conclusion appears to be that the role of dopamine in the control of ejaculatory mechanisms is unclear. Present results, together with a previous report (1), would suggest that dopamine is of little or no importance for ejaculatory mechanisms.

If enhanced dopaminergic transmission reduces mount and intromission latencies as observed, it would be reasonable to expect dopamine antagonists to increase these latencies. However, no such effect was observed. Rather, the antagonists reduced the proportion of animals showing sexual behavior, leaving the mount and intromission latencies unaffected in those animals that did copulate. It is important to note that the doses were such that no effects on motor execution, as measured by a treadmill test, could be observed, and in the case of pimozide, the lowest dose inhibiting sexual behavior is without effect on ambulatory activity as well (1). Motor deficiencies can, therefore, be excluded as the cause for the reduced sexual behavior. It is possible that dopamine exerts a permissive action on sexual behavior, i.e., below a certain dopaminergic activity level, sexual behavior cannot be activated. Above the critical level, dopamine may exert a modulatory action, controlling how rapidly this behavior is to be initiated. The fact that facilitated dopaminergic transmission reduced mount and intromission latencies without modifying the proportion of animals copulating is in agreement with this hypothesis.

While enhanced dopaminergic transmission facilitates the initiation of sexual behavior in male rats without sexual experience, no such effect could be found in experienced animals (1). Interestingly, an increase of dopamine synthesis in the nucleus accumbens during sexual activity has been found in inexperienced males, but not in males with extensive sexual experience (5). Increased levels of dopamine and DOPAC have also been found in the preoptic region of inexperienced males killed after the first intromission or after the first ejaculation (35). These data suggest a role for dopamine in sexually inexperienced males, and less so for males with sexual experience. This coincides with the present data.

It was hypothesized that dopamine becomes of importance only when environmental stimuli are critical for the initiation of sexual behavior, as is the case in animals without experience (see Introduction). Moreover, it was proposed that dopamine controls interaction with environmental stimuli in general. The experiment concerning exploratory and social behaviors was aimed to test this hypothesis. Actually, exploratory behaviors such as sniffing and rearing were facilitated by amfonelic acid, while a behavior related to sexual interaction, pursuit of the female, was not significantly modified. An increased behavioral arousal is also suggested by the observation that each event of sniffing and rearing was shorter after treatment with amfonelic acid. These data seem to suggest that stimulation of dopaminergic transmission does not specifically modify social or sexual interaction, but facilitates sexual behavior as a consequence of heightened arousal. Indeed, there is evidence that brain dopamine levels are modified by a variety of situations sharing the property of being arousing. These situations include electric shock (14), exposure to an unknown conspecific or tail-pinch (31), as well as fighting (27). Some of these situations are also sexually arousing (6,7).

The effects of flupentixol on exploratory behavior were less pronounced. Only the duration of each event of rearing was increased. It is not evident that this small effect of flupentixol on exploratory behavior can explain its effects on sexual behavior. Perhaps that the initiation of sexual behavior in inexperienced males is associated with enhanced activity of dopamine systems. If this enhancement is blocked by dopamine antagonists, no sexual behavior occurs. As suggested above dopamine may be permissive for sexual activity.

The role of noradrenaline seems to be different from that of dopamine. Increase of noradrenergic activity lengthens mount and intromission latencies, while noradrenaline depletion shortens intromission latency. In addition, DOPS reduced the number of preejaculatory intromissions. In sexually experienced males, DOPS does not reliably modify mount and intromission latencies, nor does it reduce preejaculatory intromissions (Ågmo and Fernandez, unpublished). It seems, thus, as if the effects of DOPS on sexual behavior are limited to inexperienced males. DSP4 has no effect on mount and intromission latencies in experienced males [Ågmo and Fernandez, unpublished; (20)], nor does it affect the number of preejaculatory intromissions. It appears, then, that noradrenergic as well as dopaminergic neurotransmissions affect initiation of sexual behavior only when environmental stimuli are critical. Enhanced dopaminergic activity facilitates initiation of sexual behavior, while reduced noradrenergic activity has the same effect. This coincides with the effects of these neurotransmitters on arousal or attentional mechanisms (see Introduction). However, further studies are required to substantiate the hypothesis that the actions of noradrenaline on sexual behavior are mediated by arousal mechanisms.

In conclusion, present data suggest that catecholamines are of importance for sexual arousal in males without sexual experience. Their role in experienced animals seems to be less important, as reported previously (1).

ACKNOWLEDGEMENTS

Financial support was received from the Universidad Anáhuac. The pharmaceutical companies mentioned in the Method section generously provided us with drugs. Special thanks are due to Mr. Ramón Pérez and Mr. Mario Díaz for expert technical assistance.

REFERENCES

1. Ågmo, A.; Fernandez, H. Dopamine and sexual behavior in the male rat: A reevaluation. J. Neural Transm.77:21–37; 1989.
2. Ahlenius, S.; Larsson, K. Apomorphine and haloperidol-induced effects on male rat sexual behavior: No evidence for actions due to stimulation of central dopamine autoreceptors. Pharmacol. Biochem. Behav. 21:463–466; 1984.
3. Ahlenius, S.; Larsson, K. Lisuride, LY-141865, and 8-OH-DPAT facilitate male rat sexual behavior via a non-dopaminergic mechanism. Psychopharmacology (Berlin) 83:330–334; 1984.
4. Ahlenius, S.; Engel, J.; Larsson, K. Effects of pergolide and bromocriptine on male rat sexual behavior. J. Neural Transm. 54:165–170; 1982.
5. Ahlenius, S.; Carlsson, A.; Hillegaart, V.; Hjort, S.; Larsson, K. Region-selective activation of brain monoamine synthesis by sexual activity in the male rat. Eur. J. Pharmacol. 144:77–82; 1987.
6. Barfield, R. J.; Sachs, B. D. Sexual behavior: Stimulation by painful electric shock to the skin in male rats. Science 161:392–394; 1968.
7. Barfield, R. J.; Sachs, B. D. Effect of shock on copulatory behavior in castrated male rats. Horm. Behav. 1:247–253; 1970.
8. Beach, F. A. Characteristics of masculine "sex drive." In: Jones, M. R., ed. Nebraska symposium on motivation. Lincoln: University of Nebraska Press; 1956:1–32.
9. Benkert, O.; Renz, A.; Matussek, N. Dopamine, noradrenaline and 5-hydroxytryptamine in relation to motor activity, fighting and mounting behaviour. II. L-DOPA and DL-threodihydroxyphenylserine in combination with Ro 4-4602 and parachlorophenylalanine. Neuropharmacology 12:187–193; 1973.
10. Bitran, D.; Hull, E. M. Pharmacological analysis of male rat sexual behavior. Neurosci. Biobehav. Rev. 11:365–389; 1987.
11. Butcher, L. L.; Butcher, S. G.; Larsson, K. Effects of apomorphine, (+)-amphetamine, and nialamide on tetrabenazine-induced suppression of sexual behavior in the male rat. Eur. J. Pharmacol. 7:283–288; 1969.
12. Clark, C. R.; Geffen, G. M.; Geffen, L. B. Catecholamines and attention: Animal and clinical studies. Neurosci. Biobehav. Rev. 11:341–352; 1987.
13. Clark, J. T.; Smith, E. R.; Davidson, J. M. Evidence for the modulation of sexual behavior by α-adrenoceptors in male rats. Neuroendocrinology 41:36–43; 1985.
14. Dantzer, R.; Guilloneau, D.; Mormede, P.; Herman, J. P.; Le Moal, M. Influence of shock-induced fighting and social factors on dopamine turnover in cortical and limbic areas of the rat. Pharmacol. Biochem. Behav. 20:331–335; 1984.
15. Engberg, G.; Svensson, T. H. Amphetamine-induced inhibition of central noradrenergic neurons: A pharmacological analysis. Life Sci. 24:2245–2253; 1979.
16. Ferrari, F. Sexual excitement and stretching and yawning induced by B-HT 920. Pharmacol. Res. Commun. 17:557–564; 1985.
17. Ferrari, F.; Baggio, G.; Mangiafico, V. The dopamine autoreceptor agonist B-HT 920 markedly stimulates sexual behavior in male rats. Experientia 41:636–638; 1985.
18. Foreman, M. M.; Hall, J. L. Effects of D-2 dopaminergic receptor stimulation on male rat sexual behavior. J. Neural Transm. 68: 153–170; 1987.
19. Groves, P. M.; Tepper, J. M. Neural mechanisms of action of amphetamine. In: Creese, E., ed. Stimulants: Neurochemical, behavioural and clinical perspectives. New York: Raven; 1983:81–129.
20. Hansen, S.; Kohler, C.; Ross, S. B. On the role of the dorsal mesencephalic tegmentum in the control of masculine sexual behavior in the rat: Effects of electrolytic lesions, ibotenic acid, and DSP4. Brain Res. 240:311–320; 1982.
21. Hlinak, Z.; Madlafousek, J. Initiation of copulatory behaviour in castrated male rats implanted with very small testosterone-filled silastic capsules. Endokrinologie 79:35–43; 1982.
22. Hlinak, Z.; Madlafousek, J.; Mohapelova, A. Initiation of copulatory behavior in castrated male rats injected with critically adjusted doses of testosterone. Horm. Behav. 13:9–20; 1979.
23. Hull, E. M.; Bitran, D.; Pehek, E. A.; Warner, R. K.; Band, L. C.; Holmes, G. M. Dopaminergic control of male sex behavior: Effects of an intracerebrally infused agonist. Brain Res. 370:73–81; 1986.
24. Hyttel, J. SCH 23390—The first selective dopamine D-1 antagonist. Eur. J. Pharmacol. 91:153–154; 1983.
25. Jaim-Etcheverry, G.; Ziehen, L. M. DSP-4: A novel compound with neurotoxic effects on noradrenergic neurons of adult and developing rats. Brain Res. 188:513–523; 1980.
26. Jonsson, G.; Hallman, H.; Ponzio, F.; Ross, S. DSP4 (N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine)—a useful denervation tool for central and peripheral noradrenaline neurons. Eur. J. Pharmacol. 72:173–188; 1981.
27. Kantak, K. M.; Hegstrand, L. R.; Eichelman, B. Regional changes in monoamines and metabolites following defensive aggression in the rat. Brain Res. Bull. 12:277–232; 1984.
28. Landau, J. T.; Madden, J. E. Hormonal regulation of female proceptivity and its influence on male sexual preference in rats. Physiol. Behav. 31:679–685; 1983.
29. Langer, S. Z.; Arbilla, S. The amphetamine paradox in dopaminergic neurotransmission. Trends Pharmacol. Sci. 9:387–390; 1984.
30. Larsson, K. Features of neuroendocrine regulation of masculine sexual behavior. In: Beyer, C., ed. Endocrine control of sexual behavior. New York: Raven; 1979:77–163.
31. Louilot, A.; Le Moal, M.; Simon, H. Differential reactivity of dopaminergic neurons in the nucleus accumbens in response to different behavioral situations. An in vivo voltammetric study in free moving rats. Brain Res. 397:395–400; 1986.
32. Louilot, A.; Taghzouti, K.; Deminiere, J. M.; Simon, H.; Le Moal, M. Dopamine and behavior: functional and theoretical considerations. In: Sandler, M.; Feuerstein, C.; Scatton, B., eds. Neurotransmitter interaction in the basal ganglia. New York: Raven; 1987:193–204.
33. Madlafousek, J.; Hlinak, Z. Importance of female's precopulatory behaviour for the primary initiation of male's copulatory behaviour in the laboratory rat. Behaviour 86:237–249; 1983.
34. Malmnas, C. O. Monoaminergic influence on testosterone-activated copulatory behavior in the castrated male rat. Acta Physiol. Scand. Suppl. 395:1–129; 1973.
35. Mas, M.; Rodriguez del Castillo, A.; Guerra, M.; Davidson, J. M.; Battaner, E. Neurochemical correlates of male sexual behavior. Physiol. Behav. 41:341–345; 1987.
36. Mason, S. T. Noradrenaline and selective attention: a review of the model and the evidence. Life Sci. 27:617–631; 1980.
37. Meyerson, B. J.; Hoglund, A. U. Exploratory and socio-sexual behaviour in the male laboratory rat: A methodological approach for the investigation of drug action. Acta Pharmacol. Toxicol. 48: 168–180; 1981.
38. Miller, H. H.; Shore, P. S. Effects of amphetamine and amfonelic acid on the disposition of striatal newly synthetized dopamine. Eur. J. Pharmacol. 78:33–44; 1982.
39. Napoli-Farris, L.; Fratta, W.; Gessa, G. L. Stimulation of dopamine autoreceptors elicits premature ejaculation in rats. Pharmacol. Biochem. Behav. 20:69–72; 1984.
40. Paglietti, E.; Pellegrini Quarantotti, B.; Mereu, G.; Gessa, G. L. Apomorphine and l-DOPA lower ejaculation threshold in the male rat. Physiol. Behav. 20:559–562; 1978.
41. Paredes, R.; Ågmo, A. Stereospecific actions of baclofen on sociosexual behavior, locomotor activity and motor execution. Psychopharmacology (Berlin) 97:358–364; 1989.
42. Pfaus, J. G.; Phillips, A. G. Cholecystokinin facilitates ejaculation in male rats: blockade with proglumide and apomorphine. Eur. J. Pharmacol. 141:331–338; 1987.
43. Sachs, B. D. Conceptual and neural mechanisms of masculine copulatory behavior. In: McGill, T. E.; Dewsbury, D. A.; Sachs, B. D., eds. Sex and behavior: Status and prospectus. New York: Plenum; 1978:267–295.
44. Shore, P. S. Actions of amfonelic acid and other nonamphetamine stimulants on the dopamine neuron. J. Pharm. Pharmacol. 28: 855–857; 1976.
45. Soulairac, M. L. Etude experimentale des regulations hormononerveuses du comportement sexuel du rat male. Paris: Masson; 1963.
46. Stricker, E. M.; Zigmond, N. J. Brain catecholamines and motivated behavior: Specific or nonspecific contributions? In: Usdin, E.; Carlsson, A.; Dahlstrom, A.; Engel, J., eds. Catecholamines and central nervous system—Theoretical aspects. New York: Alan R. Liss; 1984:259–269.

47. Szechtman, H. Behavior performed at onset of drug action and apomorphine stereotypy. Eur. J. Pharmacol. 121:49–56; 1986.

48. Timmermans, P. B. M. W. M.; Thoolen, M. J. M. C. Autoreceptors in the central nervous system. Med. Res. Rev. 7:307–332; 1987.