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Quinelorane (LY163502), a D2 Dopamine Receptor Agonist, Acts Centrally to Facilitate Penile Erections of Male Rhesus Monkeys

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POMERANTZ, S. M. *Quinelorane (LY163502), a D2 dopamine receptor agonist, acts centrally to facilitate penile erections of male rhesus monkeys.* PHARMACOL BIOCHEM BEHAV **39**(1) 123–128, 1991.—The present study examined the effects of a specific D2 dopamine receptor agonist, quinelorane (LY163502), on male sexual responding of rhesus monkeys. The effects of quinelorane were assessed by observing the behavioral responses of male rhesus monkeys to a sexually receptive female monkey that they could see, hear, and smell, but not physically contact. Quinelorane (IM) treatment produced dose-dependent effects on male sexual responding. Penile erections and masturbation were markedly facilitated following treatment with either 2.5 or 5 μg/kg quinelorane. Higher doses of quinelorane (10 and 25 μg/kg) generally did not further augment sexual responding, but rather resulted in a return in sexual responding to control vehicle levels. Quinelorane had a biphasic effect on yawning behavior of the monkeys with low doses (2.5 and 5 μg/kg) facilitating yawning and high doses (25 μg/kg) inhibiting yawning. Quinelorane in the dose-range (1–25 μg/kg) being evaluated did not reliably influence stereotypic behavior. In order to determine whether quinelorane acts centrally or peripherally to stimulate male sexual behavior, the ability of the peripherally active dopamine antagonist, domperidone, and the centrally active dopamine antagonist, haloperidol, to block the facilitation of sexual behavior produced by quinelorane treatment was examined. Administration of domperidone (50–200 μg/kg) failed to block quinelorane's effects on sexual behavior, whereas treatment with haloperidol (5–20 μg/kg) prevented quinelorane from stimulating male sexual responding. These experiments provide further evidence that dopaminergic mechanisms may play a role in the regulation of male sexual behavior of rhesus monkeys and, in particular, demonstrate the sexual stimulant properties of agents that provide central stimulation to D2 dopamine receptor sites.

Quinelorane Dopamine D2 receptors Male sex behavior Penile erection Rhesus monkeys Primates

RESEARCH has indicated that dopaminergic mechanisms may be involved in regulating male sexual behavior [reviewed in (5)]. In studies conducted on laboratory rats, agents which increase dopaminergic activity by stimulating either dopamine synthesis or postsynaptic dopamine receptor sites have been found to facilitate male sexual behavior, whereas agents that decrease dopaminergic activity by inhibiting either dopamine synthesis or blocking postsynaptic receptor sites have been found to reduce male sexual behavior.

Although most research examining dopaminergic involvement in male sexual behavior has been conducted on laboratory rats, recent studies in both humans and rhesus monkeys indicate that dopamine may also influence regulation of male sexual behavior in primate species. In humans, treatment with the dopamine receptor agonist, apomorphine, facilitated penile erections of both normal (19) and impotent men (20). Apomorphine also facilitated penile erections and masturbatory behavior of rhesus monkeys (26), when males were tested in the presence of a female monkey that they could see, hear and smell, but not physically contact. However, apomorphine did not alter male sexual responding when males were tested with no female present, indicating that social stimuli may interact with dopaminergic stimulation to influence male sexual behavior of rhesus monkeys.

Apomorphine stimulates both D1 (positively linked to adenylate cyclase) and D2 (negatively or not linked to adenylate cyclase) dopamine receptors (15, 16, 23, 29). Recent studies in rats indicate that dopaminergic agents that differ in their selectivity for D1 and D2 receptors may differentially affect male sexual behavior (6, 12, 14, 22). For example, it has been demonstrated in rats that whereas systemic administration of the mixed D1/D2 receptor agonist, apomorphine, stimulated penile erectile reflexes (24), systemic administration of the highly selective D2 dopamine receptor agonist, quinelorane (LY163502) (7,11), inhibited penile reflex activity (6). Thus, in light of our previous findings demonstrating the ability of apomorphine to facilitate penile erections of rhesus monkeys, the present study was designed to further investigate dopaminergic influences on male sex behavior of rhesus monkeys by examining whether administration of the selective D2 dopamine receptor agonist, quinelorane, would facilitate male sexual responding of rhesus monkeys. Additionally, the ability of the dopamine antagonists, domperidone (peripheral action only) and haloperidol (central and peripheral action) to block the effect

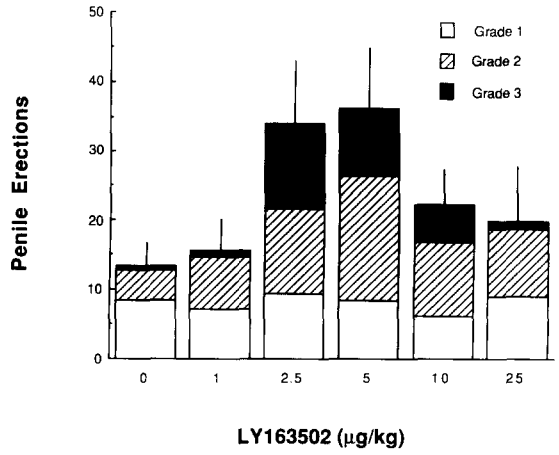

FIG. 1. Mean ± SEM number of 10-s periods in which male rhesus monkeys (N = 7) exhibited Grade 1, Grade 2 and Grade 3 penile erections following administration of varying doses of quinelorane (LY163502) (1–25 μg/kg) or saline vehicle.

of quinelorane on behavior was examined.

METHOD

Subjects

Sexually experienced adult male rhesus monkeys were used as experimental subjects. Seven males were used in both Experiments 1 and 2. In Experiment 3, six males used in Experiments 1 and 2, and two males not used previously served as subjects. A pool of four adult female rhesus monkeys served as stimulus females. Females were treated with estradiol cypionate (500 μg/week IM). This hormonal regimen maintains blood levels of estradiol around 300 pg/ml while reliably stimulating female sexual behavior (4).

Monkeys were individually housed in rooms that were temperature (18–21°C) and light controlled (12:12 light:dark with lights on at 0700 h). They were fed Purina Monkey Chow supplemented with fresh fruit. Water was available ad lib.

Apparatus

A wire mesh cage with a clear Lexan front and stainless steel partition dividing the cage into two identical compartments (0.9 × 0.8 × 0.85 m) was used as a testing cage. The floor of the cage was 0.75 m above the floor of the room. During the experiment, males lived on one side of the cage and were tested on the other side of the cage. A clear Lexan transport cage (0.75 × 0.40 × 0.70 m) with wheels mounted on the bottom was used to present the stimulus female to the males.

Behavioral Testing Procedure

The behavioral testing procedure was identical to that employed previously (26). Males were moved into the testing cage 2–4 days before an experiment began. For all experimental sessions, males were transported in the testing cage to an empty experimental room. They were removed briefly (<2 min) from the testing cage, weighed, transferred to a squeeze apparatus and injected with the appropriate treatment, and returned to the testing cage for behavioral testing in the compartment opposite to the one in which they were previously housed. In the behavioral tests, a stimulus female rhesus monkey was placed in a transport cage and wheeled into the experimental room so that she was situated approximately 0.5 m in front of the testing cage. An observer sat 1.5 m from the transport cage and for the next fifteen minutes scored the male's behavior. The 15-min test was divided into 10-s blocks, and each block in which a behavior was observed was recorded as one occurrence of that behavior. The following sexual behaviors were scored: purse-lip courtship gesture (27), penile erection, and masturbation. Penile erections were classified according to three grades of intensity: Grade 1—the glans penis visibly protruded from the penile sheath; Grade 2—the glans penis and shaft of the penis largely extended, but not fully erect; and Grade 3—penis fully erect and oriented at less than a 90° angle from the male's trunk. Although capable of exhibiting a single sustained penile erection, the monkeys never exhibited such a response in this testing situation. Rather, monkeys tended to exhibit multiple erections that varied in duration. Additionally, during the course of an erection the intensity often varied, therefore, for each 10-s period, a monkey received a score for the highest intensity of erection exhibited during that period. Nonsexual behaviors were also scored including yawning and stereotypic gnawing of a stainless steel clip-lock and chain attached to the cage. After the 15-min test was concluded, the stimulus female was returned to her home cage and the experimental male was transferred back to the testing cage compartment in which he was originally housed prior to the behavioral test. Males were maintained in the testing cage until the experiment was completed. Tests were conducted between 1400 h and 1730 h.

Experiment 1. In a counterbalanced fashion monkeys were injected (IM) daily with either quinelorane (LY163502) or saline vehicle. Each monkey was given a range of quinelorane doses in random order that included 1, 2.5, 5, 10, and 25 μg/kg quinelorane. Behavioral tests were conducted 10 min following quinelorane or vehicle injection.

Experiment 2. Monkeys were injected (IM) daily with either domperidone or 0.1 M tartaric acid vehicle. Each monkey was given a range of domperidone doses in random order that included 50, 100 and 200 μg/kg domperidone. Thirty min following the first injection, monkeys were injected with either quinelorane or saline vehicle. Doses of quinelorane were selected for each monkey based on the ability of the dose to facilitate penile erections in Experiment 1. Six males received 5 μg/kg quinelorane and one male received 10 μg/kg quinelorane. Behavioral tests were conducted 10 min following the second injection.

Experiment 3. Monkeys were injected (IM) daily with either haloperidol or 0.3% acetic acid vehicle. Each monkey was given a range of haloperidol doses in random order that included 5, 10, and 20 μg/kg haloperidol. Fifty min following the first injection, monkeys were injected with either quinelorane or saline vehicle. Doses of quinelorane were selected for each monkey based on the ability of the dose to facilitate penile erections. Six males received 5 μg/kg quinelorane, and two males received 2.5 μg/kg quinelorane. Behavioral tests were conducted 10 min following the second injection.

Data Analysis

In each experiment, one-way analysis of variance (ANOVA) tests were conducted to determine whether repeated testing of the monkeys influenced their behavior in vehicle tests. Since no effects of repeated testing were found for any of the behaviors being assessed, for each behavior the males' mean score in vehicle tests was used in subsequent analyses aimed at evaluating the effects of the different drug treatments. For these analyses, repeated measures one-way ANOVA tests were conducted. Analyses yield-

TABLE 1

EFFECTS OF QUINELORANE ON BEHAVIOR OF RHESUS MONKEYS IN SEXUAL STIMULUS TESTS

Quinelorane* (μg/kg)	Masturbation	Purse-Lip Gestures	Yawns	Gnaw
0	0.1(0.1)	5.7(1.2)	7.3(2.1)	1.4(1.4)
1.0	0.7(0.6)	4.5(0.5)	7.1(2.3)	0.9(0.9)
2.5	3.4(1.8)[b]	3.6(0.8)	12.6(2.5)[a]	0.0(0.0)
5.0	5.4(1.9)[b]	6.5(1.4)	12.0(1.6)[a]	0.8(0.7)
10	3.1(1.5)[b]	4.9(0.9)	5.7(1.3)	6.3(4.8)
25	1.0(0.7)	6.3(1.4)	2.0(1.0)[a]	5.0(3.2)

*Values represent mean(±SEM) number of 10-s periods in which behaviors were observed.

[a]$p<0.01$ relative to vehicle-treated monkeys.

[b]$p<0.05$ relative to vehicle-treated monkeys.

ing significant overall effects were followed by posthoc comparisons using the Duncan multiple range test (30).

RESULTS

Experiment 1

As shown in Fig. 1, quinelorane produced a dose-dependent stimulation of penile erection. The effect of quinelorane on the total sum of all three grades of penile erection was significant, $F(5,30)=5.55$, $p<0.01$. Further analysis revealed that quinelorane significantly influenced performance of Grade 2 and 3 erections, $F(5,30)=5.02$, $p<0.01$, but not Grade 1 erections ($F<1.0$). Compared to vehicle treatment, the facilitation of penile erections by quinelorane was statistically reliable at 2.5 and 5 μg/kg quinelorane ($p<0.01$). However, following treatment with 25 μg/kg quinelorane, a significant decline in penile erections was observed ($p<0.05$), such that monkeys were performing at a level that did not differ significantly from their performance under vehicle conditions.

The effects of quinelorane on other behaviors assessed in this testing situation are shown in Table 1. The frequency of masturbatory behavior in monkeys administered 2.5, 5 and 10 μg/kg quinelorane was significantly higher than when they were administered vehicle, $F(5,30)=3.06$, $p<0.05$. Masturbation proceeded to an ejaculation in one male following treatment with both 2.5 and 5 μg/kg quinelorane, another monkey ejaculated following treatment with 5 μg/kg quinelorane and one male ejaculated following treatment with 10 μg/kg quinelorane. No ejaculations were observed when the males were administered vehicle treatment.

Quinelorane produced a biphasic effect on yawning, $F(5,30)=8.87$, $p<0.001$. Compared to vehicle based performance, yawning was significantly increased in monkeys treated with 2.5 and 5 μg/kg quinelorane, and was significantly decreased in monkeys treated with 25 μg/kg quinelorane. Quinelorane did not significantly influence performance of purse-lip courtship gestures, $F(5,30)=1.8$, $p>0.05$, or stereotypic gnawing behavior, $F(5,30)=1.16$, $p>0.05$. Regarding induction of stereotypic behavior, it should be noted that although most monkeys did not exhibit signs of stereotypy, in two monkeys some gnawing behavior emerged following 10 μg/kg quinelorane and in another monkey gnawing behavior was observed following 25 μg/kg quinelorane. None of these monkeys exhibited signs of stereotypic gnawing behavior following either vehicle treatment or lower doses of quinelorane. No locomotor stereotypies were observed at the dosages of quinelorane used in this experiment.

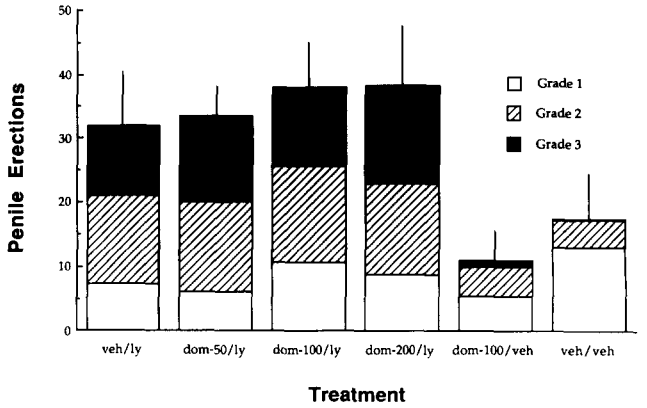

FIG. 2. Mean ± SEM number of 10-s periods in which male rhesus monkeys (N = 7) exhibited Grade 1, Grade 2 and Grade 3 penile erections following administration of varying doses of domperidone (dom) (50, 100 and 200 μg/kg) or 0.1 M tartaric acid vehicle (veh) forty min prior to testing and quinelorane (ly) or saline vehicle (veh) ten min prior to testing.

Experiment 2

The effects of domperidone and quinelorane treatment on the behavior of the monkeys are shown in Fig. 2 and Table 2. Experimental treatments significantly influenced the monkeys' performance of penile erections, $F(5,30)=7.53$, $p<0.001$, and masturbatory behavior, $F(5,30)=3.93$, $p<0.01$. Post hoc comparisons revealed that regardless of domperidone treatment, monkeys receiving quinelorane exhibited significantly more penile erections ($p<0.01$, Fig. 2) and masturbatory behavior ($p<0.05$, Table 2) than monkeys that did not receive quinelorane. Administration of domperidone (50–200 μg/kg) did not affect the facilitation of penile erections and masturbatory behavior produced by quinelorane. Additionally, domperidone did not interfere with quinelorane's facilitation of yawning behavior. Finally, no significant behavioral effects of domperidone alone were observed.

In order to try to confirm that the dosages of domperidone being employed were capable of inhibiting known dopamine actions on peripheral tissues, the effect of domperidone on prolac-

TABLE 2

EFFECTS OF QUINELORANE AND DOMPERIDONE ON BEHAVIOR OF RHESUS MONKEYS IN SEXUAL STIMULUS TESTS

Treatment*	Masturbation	Yawns
vehicle + quinelorane	5.6(1.3)[b]	8.9(1.9)[b]
50 μg/kg domperidone + quinelorane	9.0(3.5)[a]	10.5(2.8)[b]
100 μg/kg domperidone + quinelorane	8.3(2.9)[a]	12.4(1.2)[b]
200 μg/kg domperidone + quinelorane	6.5(2.1)[b]	10.8(2.7)[b]
100 μg/kg domperidone + vehicle	0.9(0.9)	4.9(2.0)
vehicle + vehicle	0.1(0.1)	5.8(1.7)

*Values represent mean(±SEM) number of 10-s periods in which behaviors were observed.

[a]$p<0.01$ relative to vehicle + vehicle-treated monkeys.

[b]$p<0.05$ relative to vehicle + vehicle-treated monkeys.

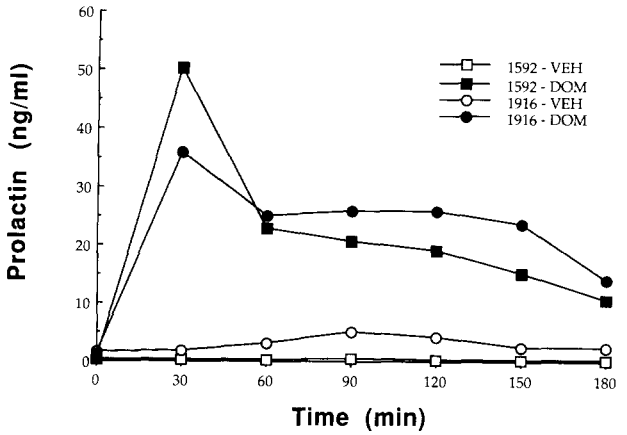

FIG. 3. Prolactin secretion in blood samples taken every 30 min from male monkeys 1592 and 1916. Each monkey had an indwelling venous catheter and was fitted with a jacket/tether/swivel system to allow remote blood sample collection. On alternate days monkeys were treated with either 100 μg/kg domperidone (DOM) or 0.1 M tartaric acid (VEH) immediately following the blood sample taken at 0 min.

tin secretion (2) was examined (in collaboration with Dr. Judy Cameron, University of Pittsburgh School of Medicine). Two adult male rhesus monkeys with indwelling venous catheters and outfitted with a jacket/tether/swivel system to allow remote blood sample collection were sampled folowing IM administration of either 100 μg/kg domperidone or 0.1 M tartaric acid vehicle. As shown in Fig. 3, 100 μg/kg domperidone markedly stimulated prolactin release in both monkeys.

Experiment 3

The effects of haloperidol and quinelorane treatment on the behavior of the monkeys are shown in Fig. 4 and Table 3. Treatment of the monkeys with haloperidol blocked in a dose-dependent manner the facilitation of penile erections, $F(5,35) = 30.0$, $p<0.001$, produced by quinelorane (Fig. 4). Post hoc

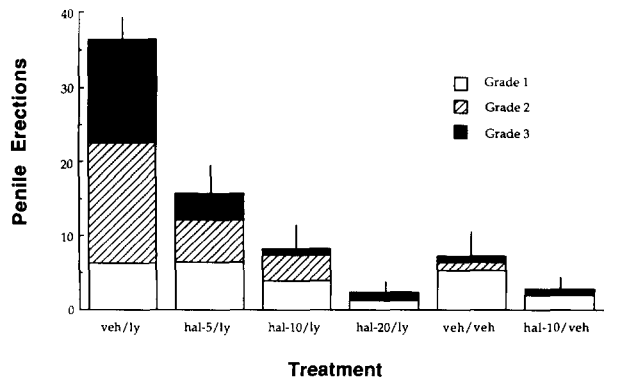

FIG. 4. Mean ± SEM number of 10-s periods in which male rhesus monkeys (N = 8) exhibited Grade 1, Grade 2 and Grade 3 penile erections following administration of varying doses of haloperidol (hal) (5, 10 and 20 μg/kg) or 0.3% acetic acid vehicle (veh) sixty min prior to testing and quinelorane (ly) or saline vehicle (veh) ten min prior to testing.

TABLE 3

EFFECTS OF QUINELORANE AND HALOPERIDOL ON BEHAVIOR OF RHESUS MONKEYS IN SEXUAL STIMULUS TESTS

Treatment*	Masturbation	Yawns	Purse-Lip Gestures
vehicle + quinelorane	8.1(1.6)	14.2(3.0)	2.5(0.7)
5 μg/kg haloperidol + quinelorane	2.1(0.4)[b]	10.4(4.0)	3.4(1.2)
10 μg/kg haloperidol + quinelorane	2.1(1.1)[b]	7.9(3.5)[c]	2.9(0.9)
20 μg/kg haloperidol + quinelorane	0.4(0.4)[b]	4.3(3.0)[a,b]	4.1(1.3)
10 μg/kg haloperidol + vehicle	0.3(0.3)[b]	6.8(2.4)[c]	5.2(1.3)
vehicle + vehicle	0.6(0.4)[b]	9.8(2.9)	3.6(1.2)

*Values represent mean(±SEM) number of 10-s periods in which behaviors were observed.
[a]$p<0.05$ relative to vehicle + vehicle-treated monkeys.
[b]$p<0.01$ relative to vehicle + quinelorane-treated monkeys.
[c]$p<0.05$ relative to vehicle + quinelorane-treated monkeys.

comparisons revealed that haloperidol treatment significantly inhibited both Grade 2 and Grade 3 penile erections of monkeys receiving quinelorane ($p<0.01$), while Grade 1 erections were not significantly affected by haloperidol treatment ($p>0.05$). Performance of penile erections by monkeys receiving 5 μg/kg haloperidol plus quinelorane was intermediate between that of monkeys treated with vehicle plus quinelorane ($p<0.05$) and monkeys receiving either 10 or 20 μg/kg haloperidol plus quinelorane ($p<0.05$). As shown in Table 3, haloperidol treatment at all dosage levels significantly reduced masturbatory behavior compared to monkeys that received haloperidol vehicle followed by quinelorane, $F(5,35) = 12.5$, $p<0.001$.

A significant treatment effect on yawning behavior was observed, $F(5,35) = 3.54$, $p<0.01$, with monkeys receiving either 10 or 20 μg/kg haloperidol plus quinelorane exhibiting significantly fewer yawns than monkeys treated with haloperidol vehicle plus quinelorane (Table 3). It should be noted that in this experiment, the yawning behavior of monkeys receiving vehicle followed by quinelorane did not differ statistically from their behavior in tests in which they received dual vehicle injections. One animal accounts for this lack of effect, as his yawning under vehicle treatments was higher than that following quinelorane treatment. In the seven other monkeys tested, quinelorane treatment in the absence of haloperidol resulted in an increase in yawning over dual vehicle injections. The various drug treatments did not significantly influence performance of courtship purse-lip gestures.

DISCUSSION

The results of this experiment demonstrate that treatment of male rhesus monkeys with the specific dopamine D2 receptor agonist, quinelorane, produced dose-dependent effects on male sexual responding. Penile erections and masturbation were markedly facilitated following treatment with either 2.5 or 5 μg/kg quinelorane. Higher doses of quinelorane generally did not further augment sexual responding, but rather resulted in a return in sexual responding to control vehicle levels. Additionally, quinelorane appeared to facilitate sexual behavior by acting centrally, since domperidone, a peripherally acting dopamine antagonist (17), failed to block quinelorane's effects, whereas haloperidol, a centrally acting dopamine receptor antagonist,

prevented quinelorane from stimulating male sexual responding.

The results with quinelorane complement previous research from this laboratory in which apomorphine treatment of male rhesus monkeys also yielded biphasic response curves for both penile erections and masturbatory behavior (26). Further comparison of the results across these two studies indicates that quinelorane was approximately 20–50 times more potent than apomorphine in facilitating both penile erection and masturbatory behavior. Quinelorane, unlike apomorphine, did not reliably elicit stereotypic behavior at high doses that failed to facilitate male sexual responding. Nevertheless, the highest quinelorane dose being evaluated was still substantially less than the dose of apomorphine (200–400 μg/kg) needed to elicit stereotypic behavior. Thus future studies may have to evaluate the behavior of monkeys given doses of quinelorane above 25 μg/kg to determine whether stereotypic behavior in rhesus monkeys can be elicited following stimulation of only D2 dopamine receptors or whether stimulation of both D1 and D2 receptors is needed to produce behavioral stereotypies.

Since studies in rats have also indicated that dopaminergic mechanisms may be involved in the regulation of penile erection (1, 13, 24), it is important to compare the results obtained in both the rat and monkey studies conducted to date. The mixed D1/D2 agonist, apomorphine, facilitated penile erections in both species. However, whereas specific D2 receptor stimulation with quinelorane potently facilitated male penile erections in rhesus monkeys, quinelorane had an inhibitory effect on penile erectile reflexes of rats following either systemic administration or central administration into the medial preoptic area (6). Although these findings point to an apparent species difference in the effect of D2 receptor stimulation on penile erections, it is important to note that methodological differences in conducting these studies in the two species might also be responsible for producing the species differences in the effect of D2 receptor stimulation on penile erections. We previously demonstrated that in monkeys the stimulation of penile erections by apomorphine was dependent on the presence of the female in the testing situation (26). Without the female being present, apomorphine failed to stimulate penile erections. A similar effect of the female on the induction of penile erections by quinelorane in rhesus monkeys has also been reported (9). By contrast, in rats the facilitation of penile erection by apomorphine can occur while the animal is freely moving in the absence of any social stimulus (1,13) or with the rat restrained in a supine position (24). Effects of dopaminergic agents on rodent penile erections have not yet been evaluated in a social situation. Thus, without conducting similar tests of the effects of dopaminergic agents in both species, it is difficult to arrive at any firm conclusions regarding possible species differences in dopaminergic influences on penile erections.

Research with rats has also found that quinelorane stimulated seminal emission (6). On the basis of these results it has been suggested that the ability of quinelorane to facilitate penile erections of rhesus monkeys may be due to a similar stimulation of seminal emission in monkeys. Nonetheless, data collected thus far do not support this conclusion. We did not observe any instances in which the monkeys exhibited spontaneous seminal emissions. Additionally, although in some cases quinelorane facilitated masturbatory behavior resulting in ejaculation with seminal emission, more typically monkeys exhibited a quinelorane-dependent increase in masturbatory behavior that was not accompanied by an ejaculation. Regarding quinelorane's ability to facilitate both penile erection and masturbatory behavior, it should be noted that these two behaviors were not mutually exclusive. Although masturbation was always associated with a penile erection, penile erections were not necessarily associated with masturbation. Furthermore, on occasions in which the monkeys exhibited masturbatory behavior, they would not generally begin to masturbate until after they had achieved a penile erection.

Facilitation of male sexual responding by quinelorane was prevented by prior administration of haloperidol, but not domperidone. Since both compounds act peripherally to antagonize dopamine activity, but only haloperidol has significant dopamine antagonist activity centrally, these results indicate that quinelorane is acting centrally to facilitate penile erections and masturbatory behavior in rhesus monkeys. These results are consistent with both rat (12, 13, 24) and human (18,21) studies demonstrating that centrally active dopamine antagonists such as haloperidol, pimozide and sulpiride, but not the peripherally active dopamine antagonist, domperidone, were able to block the ability of dopamine agonists to facilitate male sexual responding. Additionally, the observation that purse-lip gestures were unaffected by haloperidol treatments indicates that haloperidol was acting specifically to block those behaviors that were facilitated by quinelorane treatment (i.e., penile erections, masturbation and yawning) and was not exerting its effects by merely producing a generalized debilitation of the animal.

Quinelorane administration to rhesus monkeys facilitated yawning at doses which also led to a potentiation of penile erections, and inhibited yawning at doses in which its effect on penile erections had waned. Additionally, the stimulatory effects of quinelorane on yawning and penile erections were blocked by haloperidol, but not by domperidone. These data are consistent with other studies in rats (13, 22, 28), humans (18) and monkeys (26) indicating that dopaminergic stimulation may influence both penile erection and yawning responses in a parallel fashion. Although both yawning and penile erections respond in a similar fashion to pharmacological alterations of dopaminergic activity, the functional significance of having these two seemingly unrelated behaviors both be modulated by similar dopaminergic mechanisms is not readily apparent and needs to be addressed in the future. In this regard, it may be worth noting that androgens also exert a parallel effect on both sexual behavior and yawning of rhesus monkeys (25), and in mating situations male rhesus monkeys frequently exhibit yawns both prior to copulation and immediately after copulatory mounts of the female (Pomerantz, unpublished observations). Thus yawning may be part of the sexual response of male rhesus monkeys and, as such, those yawns that occur in a sexual context may share a similar neurochemical substrate with other male sexual behaviors.

The results of the present study indicate that specific D2 dopamine receptor stimulation with agents such as quinelorane may provide a useful pharmacotherapy in cases of male sexual dysfunction. In particular, quinelorane may prove beneficial in treating male sexual impotence associated with inability to either achieve or maintain a penile erection. The aim of any such treatment would be to manipulate central mechanisms involved in the regulation of penile erection. This approach can be contrasted against treatments that are directed at peripheral mechanisms regulating penile erection and involve direct intrapenile injection of smooth muscle relaxants into the corpora cavernosa (3). Finally, it should be noted that although quinelorane has been found to facilitate penile erections of rhesus monkeys, the effects of this compound on copulatory behavior of male rhesus monkeys have not yet been evaluated. Since the mixed D1/D2 receptor agonist, apomorphine, has been studied and been found to either inhibit or have no effect on male copulatory behavior of rhesus monkeys (8,10), it will be important that future investigations examine the effects of quinelorane on male copulatory performance of rhesus monkeys.

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