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Yohimbine interacts with the dopaminergic system to reverse sexual satiation: further evidence for a role of sexual motivation in sexual exhaustion

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Abstract

The possible interaction of yohimbine with the dopaminergic system in the mediation of sexual behaviour expression in sexually exhausted male rats was investigated. The behavioural effects of the simultaneous injection of yohimbine (500 μg/kg) plus apomorphine (50 μg/kg) and those of the combined treatment of haloperidol (125 μg), a nonspecific dopamine receptor antagonist, with an effective dose of yohimbine (2000 μg/kg) on sexually satiated rats were evaluated. Data show that yohimbine and apomorphine, per se, dose-dependently reverse sexual exhaustion by increasing the percentage of sexually satiated rats copulating and resuming copulation after ejaculation. Injection of haloperidol simultaneous to an effective dose of yohimbine, blocked the ability of the latter to reverse sexual satiation. The combined treatment with subthreshold doses of apomorphine and yohimbine synergised to reverse the sexual inhibition characteristic of sexual exhaustion. Data suggest that the dopaminergic system might be the final pathway for the yohimbine-induced sexual behaviour expression in satiated rats. The possible role of sexual motivation in the sexual exhaustion phenomenon is discussed.

Keywords: Yohimbine; Sexual exhaustion; Dopamine-noradrenaline interaction; Sexual behavior, male rat; Sexual motivation

1. Introduction

The sexual exhaustion state consists of a prolonged sexual behaviour inhibition (up to 72 h) that appears in response to repeated ejaculation in the course of sustained ad libitum copulation. This phenomenon was initially described by two independent groups in the early sixties (Beach and Jordan, 1956; Larsson, 1956). Although different paradigms have been used to render male rats sexually exhausted, a common feature to all is the finding that a median number of seven successive ejaculatory series is required to achieve sexual satiation (Beach and Jordan, 1956; Larsson, 1956; Lawrence and Barfield, 1975; Rodríguez-Manzo and Fernández-Guasti, 1994; Mas et al., 1995b). In our laboratory, a paradigm that consists in allowing sexually experienced male rats a four hour period of ad libitum copulation with a single female and testing the animals 24 h later for sexual behaviour has been used. This particular paradigm revealed that 24 h after copulation to exhaustion, male rats express sexual satiation in two different manners: two thirds of the population do not respond to the presence of an oestrus female and the remaining third is able to achieve only one ejaculation after which copulation is not resumed (Rodríguez-Manzo and Fernández-Guasti, 1994).

Recently, pharmacological manipulations were carried out in an attempt to identify the neurotransmitter systems that might be involved in the regulation of the sexual inhibition that characterises sexual exhaustion (Pfaus and Gorzalka, 1987; Rodríguez-Manzo and Fernández-Guasti, 1994, 1995a; Mas et al., 1995b). These studies showed that the systemic injection of a variety of drugs, acting at different neurotransmitter systems, can reverse to a significant degree this sexual refractoriness (Rodríguez-Manzo and Fernández-Guasti, 1994, 1995a; Mas et al., 1995b). In

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our paradigm this reversal is manifested by a significant increase in the percentage of satiated rats that achieve ejaculation and resume copulation after ejaculation (Rodríguez-Manzo and Fernández-Guasti, 1994).

The nonselective dopamine receptor agonist apomorphine and the α_2-adrenoceptor antagonist yohimbine, are two of the drugs that have been shown to induce mating behaviour in sexually exhausted rats (Rodríguez-Manzo and Fernández-Guasti, 1994; Mas et al., 1995b). Subsequent studies demonstrated that in noradrenaline depleted, sexually exhausted animals, yohimbine treatment was still able to markedly increase the percentage of sexually satiated males mounting, intromitting and showing the motor pattern of ejaculation (Rodríguez-Manzo and Fernández-Guasti, 1995b). This datum led us to presume that yohimbine should be acting through the interaction with a neurotransmitter system distinct from noradrenaline to induce sexual behaviour expression in sexually exhausted rats.

Neurochemical measurements in mating animals have consistently shown copulation-related increases in dopamine release and metabolism in brain areas known to participate in the expression of male rat sexual behaviour, such as the nucleus accumbens (Mas et al., 1990; Pfaus et al., 1990b; Pleim et al., 1990; Damsma et al., 1992; Wenkstern et al., 1993) and the medial preoptic area (Bitran et al., 1988; Mas et al., 1995a; Sato et al., 1995). There are also reports showing increases in dopamine metabolites' levels specifically associated to copulation to exhaustion (Pfaus et al., 1990a; Mas et al., 1995a; Fiorino et al., 1997). Finally, we recently demonstrated a blockade of the establishment of the sexual inhibition resulting from copulation to exhaustion by changing the stimulus female to sexually exhausted rats (Rodríguez-Manzo, 1999) that is not mediated by the noradrenergic system. Altogether, these data led us to presume that the participation of the noradrenergic system in the reversal of sexual exhaustion is secondary to another neurotransmitter system, presumably the central dopaminergic system. Thus, we hypothesised that yohimbine, an α_2-adrenoceptor antagonist, might be acting through an interaction with the dopaminergic system to induce sexual behaviour expression in satiated male rats.

To test this hypothesis we conducted two main series of experiments: one aimed to block the yohimbine-induced sexual behaviour expression in sexually exhausted rats with haloperidol (a nonselective dopamine receptor antagonist) and another directed to establish if the simultaneous injection of suboptimal doses of yohimbine and apomorphine (a dopamine receptor agonist) were able to synergise to reverse sexual exhaustion. Dose–response effects of haloperidol, apomorphine and yohimbine treatments on sexual behaviour expression of sexually sated males were also conducted. Finally, a spontaneous ambulatory behaviour test after each treatment was done to be able to discard unspecific motor effects of the pharmacological treatments.

2. Materials and methods

2.1. Animals

Sexually experienced adult male Wistar rats (300–350 g b.wt) were used. Animals were housed, five per cage, in a room under inverted light:dark conditions (12 h light/12 h dark; lights on at 2200 h) and with free access to commercial rat chow and tap water. All experimental procedures were performed under approval of our institutional Ethics Committee. Previous to experimental testing, all animals received three sexual behaviour tests and the sexually active males (those showing an ejaculation latency shorter than 15 min in the last of these tests, for definition vide infra) were selected for the study. Receptive female rats were used as stimuli. Receptivity was induced by the sequential s.c. injection of oestradiol valerianate (4 μg/rat) followed 44 h later by progesterone (2000 μg/rat).

2.2. Drugs

The following drugs were used: Apomorphine hydrochloride, haloperidol and yohimbine hydrochloride. All drugs were purchased from Sigma, St. Louis, USA. Apomorphine and yohimbine were dissolved in distilled water, haloperidol was dissolved in a solution of distilled water and 0.1% ascorbic acid.

2.3. Sexual behaviour observations

Sexual behaviour tests were conducted 3 h after the onset of darkness and 4 h after progesterone injection to the females. Male rats were introduced in a cylindrical observation cage and a 5 min period of adaptation allowed before introducing a single receptive female. Sexual behaviour observations were conducted in a room under dim red light and the observer was blind to the treatments. The sexual behaviour parameters registered were: (a) intromission latency: time from the introduction of the female into the observation cage to the occurrence of the first intromission; (b) number of mounts; (c) number of intromissions; (d) ejaculation latency: time from the first intromission to ejaculation; (e) postejaculatory interval: time from ejaculation to the next intromission and (f) percentage of copulating rats: proportion of subjects in each group that shows the different sexual behaviour responses, i.e., mount, intromission, ejaculation and copulation resumption after ejaculation.

2.4. Sexual exhaustion paradigm

Sexually experienced male rats were subjected to a 4 h session of ad libitum copulation with a single stimulus female (vide supra), a period proven to be sufficient to render all rats sexually exhausted (Rodríguez-Manzo and Fernández-Guasti, 1994). Twenty four hours later the same

animals were tested for sexual behaviour with a new receptive female preceded by the pharmacological treatments. This last observation was ended ensuing the following criteria: (a) a period of 30 min without showing sexual behaviour; (b) 30 min from the first intromission without achieving ejaculation; (c) 30 min after ejaculation or (d) after the first intromission from a second ejaculatory series.

2.5. Pharmacological manipulations

2.5.1. Experiment 1. Dose–response effects

A dose–response relationship was established for each drug used. Thus, yohimbine [0 μg/kg (vehicle 2 ml/kg, $n = 10$), 500 μg/kg ($n = 7$), 1000 μg/kg ($n = 8$) and 2000 μg/kg ($n = 10$); −30 min], apomorphine [0 μg/kg (vehicle 2 ml/kg, $n = 8$), 50 μg/kg ($n = 8$), 100 μg/kg ($n = 8$) and 200 μg/kg ($n = 8$); −15 min] and haloperidol [0 μg/kg (vehicle 2 ml/kg, $n = 8$), 125 μg/kg ($n = 8$) and 250 μg/kg ($n = 8$); −30 min] were i.p. injected the day after copulation to exhaustion previous to sexual behaviour testing.

2.5.2. Experiment 2. Combined injection of yohimbine and haloperidol

Two independent groups of sexually exhausted rats were tested for sexual behaviour after the following treatments:

Group 1: vehicle (2 ml/kg, i.p.), $n = 18$

Group 2: yohimbine (2000 μg/kg) plus haloperidol (125 μg/kg), i.p. −30 min, $n = 18$

2.5.3. Experiment 3. Combined injection of yohimbine plus apomorphine

Two independent groups of sexually exhausted rats were tested for sexual behaviour after the following treatments:

Group 3: vehicle (2 ml/kg, i.p.), $n = 18$

Group 4: yohimbine (500 μg/kg) plus apomorphine (50 μg/kg), i.p. −30 min, $n = 7$

2.6. Spontaneous ambulatory behaviour

All rats were tested for spontaneous ambulation immediately after the sexual behaviour testing that followed each pharmacological treatment. This was recorded in a box measuring 43 × 36 × 19 cm that was placed over a sensitive plaque (48 × 40 cm) of an activity meter (Stoelting, Chicago, IL) connected to a counter (Stoelting). The animals were placed in the cage and the number of counts recorded over a 10 min period. Between each test the cage was carefully cleaned. The data are expressed as counts/10 min.

2.7. Statistical analysis

The proportion of animals showing mounts, intromissions, ejaculating and resuming copulation after ejaculation

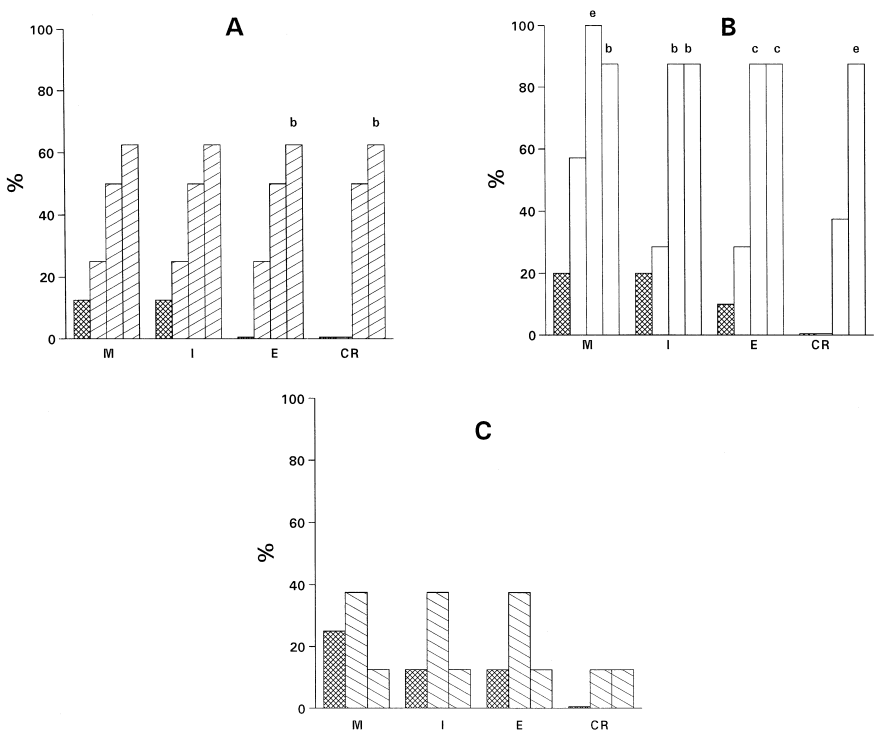

Fig. 1. Percentage of sexually exhausted rats that are able to mount (M), intromit (I), ejaculate (E) and resume copulation after ejaculation (CR) following increasing doses of apomorphine (A), yohimbine (B) and haloperidol (C). Panel A: vehicle (2 ml/kg, $n = 8$, double dashed bar) and apomorphine [50 μg/kg ($n = 8$), 100 μg/kg ($n = 8$), 200 μg/kg ($n = 8$), dashed bars]. Panel B: vehicle (2 ml/kg, $n = 10$, double dashed bar) and yohimbine [500 μg/kg ($n = 7$), 1000 μg/kg ($n = 8$), 2000 μg/kg ($n = 8$), white bars]. Panel C: vehicle (2 ml/kg, $n = 8$, double dashed bar) and haloperidol [125 μg/kg ($n = 8$), 250 μg/kg ($n = 8$), reverse dashed bars]. Fisher F-test, $^{b}P < 0.02$, $^{c}P < 0.01$, $^{e}P < 0.001$ vs. their respective control.

was established for the experimental and their proper vehicle-treated groups and statistically evaluated by means of the Fisher *F*-test (Siegel, 1965). The specific sexual behaviour parameters were determined only for those animals attaining ejaculation in the postexhaustion test (yohimbine 2000 μg/kg vs. apomorphine 50 μg/kg + yohimbine 500 μg/kg) and statistically compared by means of the Mann–Whitney *U*-test. Finally, the data regarding motor activity from the experimental groups were compared with those of their proper control by means of a one way analysis of variance (ANOVA) followed by Dunnet's *t*-test (Steel and Torrie, 1985).

3. Results

3.1. Experiment 1. Dose–response effects

Fig. 1 shows the proportion of sexually exhausted rats that were able to show each of the sexual behaviour responses (i.e., mount, intromission, ejaculation and copulation resumption) in response to different doses of apomorphine, yohimbine and haloperidol. It was found that apomorphine was able to increase the percentage of copulating sexually satiated rats in a dose-dependent fashion (panel A). These increases reached statistical significance only at the highest dose level (200 μg/kg) in the proportion of animals achieving ejaculation and reinitiating copulation after ejaculation (Fisher *F*-test, $P < 0.02$) when compared to vehicle treated animals.

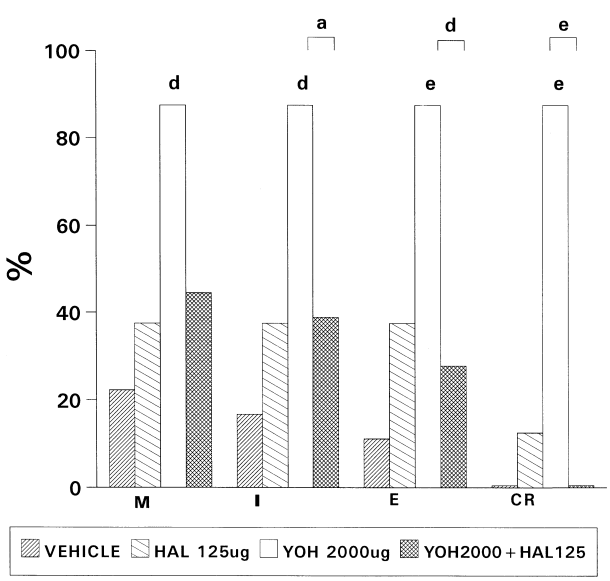

Fig. 2. Percentage of sexually exhausted rats that are able to mount (M), intromit (I), ejaculate (E) and resume copulation after ejaculation (CR) following vehicle- (2 ml/kg, $n = 18$, dashed bar), haloperidol- (125 μg/kg, $n = 8$, reverse dashed bar), yohimbine- (2000 μg/kg, $n = 8$, white bar) and the combined treatment of haloperidol plus yohimbine (125 μg/kg and 2000 μg/kg, respectively; $n = 18$, double dashed bar). Fisher *F*-test, $^{a}P < 0.05$, $^{d}P < 0.002$, $^{e}P < 0.001$. Significances over columns indicate statistical comparisons vs. control group, other comparisons are indicated by brackets.

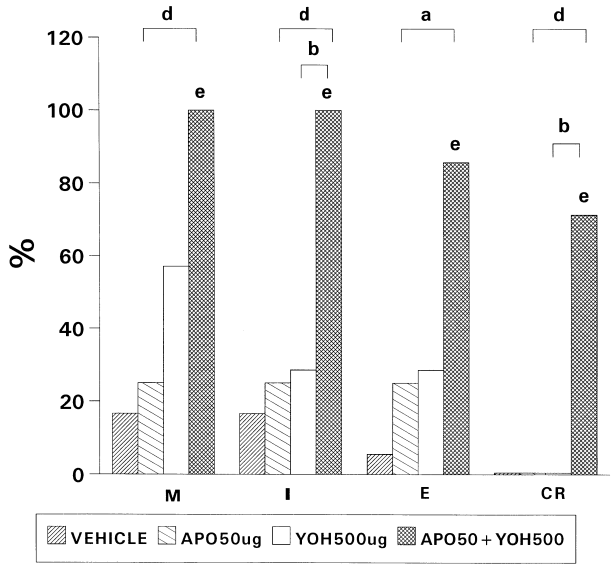

Fig. 3. Percentage of sexually exhausted rats that are able to mount (M), intromit (I), ejaculate (E) and resume copulation after ejaculation (CR) following vehicle- (2 ml/kg, $n = 18$, dashed bar), apomorphine- (50 μg/kg, $n = 8$, reverse dashed bar), yohimbine- (500 μg/kg, $n = 7$, white bar) and the combined treatment of apomorphine plus yohimbine (50 μg/kg and 500 μg/kg, respectively; $n = 7$, double dashed bar). Fisher *F*-test, $^{a}P < 0.05$, $^{b}P < 0.02$ $^{d}P < 0.002$, $^{e}P < 0.001$. Significances over columns indicate statistical comparisons vs. control group, other comparisons are indicated by brackets.

As to the effect of yohimbine injection (panel B) all doses, but the lowest (500 μg/kg), were able to significantly increase the proportion of satiated rats showing mounts, intromissions (Fisher *F*-test, $P < 0.02$) and achieving ejaculation (Fisher *F*-test, $P < 0.01$) as compared with vehicle-treated animals. Only the highest dose level (2000 μg/kg) significantly increased the percentage of exhausted rats reinitiating copulation after ejaculation (Fisher *F*-test, $P < 0.001$).

Finally, haloperidol treatment failed to reverse the sexual inhibition that characterises sexual exhaustion at the two dose levels used (panel C). The highest dose induced motor alterations in some animals (circling behaviour), precluding the testing of higher doses of this drug. The smaller proportion of copulating subjects found at the highest dose level was associated to the appearance of motor disturbances, since the affected animals were unable to copulate.

3.2. Experiment 2. Combined injection of yohimbine and haloperidol

The results obtained after the combined injection of yohimbine and haloperidol to sexually exhausted animals are shown in Fig. 2. It can be observed that haloperidol

Table 1
Specific sexual behaviour parameters of sexually exhausted rats

Treatment (μg/kg)	*n*	Intromission latency mean ± S.E.	Mounts median	Intromissions median	Ejaculation latency mean ± S.E.	Postejaculatory interval mean ± S.E.
Yohimbine 2000	7	4.60 ± 2.00	3	7	7.86 ± 1.21	21.77 ± 1.32
Yohimbine 500 + apomorphine 50	6	3.18 ± 1.22	1.5	11.5	6.08 ± 1.12	25.36 ± 1.30

injection (125 μg/kg, dashed bars), per se, did not induce mating behaviour in sexually satiated rats. Otherwise, yohimbine treatment (2000 μg/kg, white bars) significantly increased the proportion of satiated animals showing mounts, intromissions (Fisher *F*-test, $P < 0.002$), ejaculating and reinitiating copulation after ejaculation (Fisher *F*-test, $P < 0.001$) when compared with control (vehicle-injected 2 ml/kg, black bars) sexually exhausted males. Finally, when both drugs, at the same doses, were simultaneously injected (double-dashed bars), haloperidol blocked the yohimbine-induced increases in the percentages of exhausted rats intromitting (Fisher *F*-test, yohimbine + haloperidol vs. yohimbine, $P < 0.05$), ejaculating ($P < 0.002$) and reinitiating copulation after ejaculation ($P < 0.001$).

3.3. Experiment 3. Combined injection of yohimbine plus apomorphine

Fig. 3 depicts the effect of the combined administration of subthreshold doses of yohimbine (500 μg/kg) and apomorphine (50 μg/kg) on the sexual behaviour responses of sexually sated males. Figure shows that, at the dose levels used, neither apomorphine (dashed bars) nor yohimbine (white bars) were capable, per se, of inducing sexual behaviour in satiated rats. However, when injected simultaneously, both drugs synergised to induce sexual behaviour expression in sexually exhausted males. Thus, after this treatment, 100% of the subjects was able to mount (Fisher *F*-test, $P < 0.001$ vs. vehicle; $P < 0.002$ vs. apomorphine) and intromit ($P < 0.001$ vs. vehicle, $P < 0.002$ vs. apomorphine and $P < 0.02$ vs. yohimbine), 90% ejaculated ($P < 0.001$ vs. vehicle, $P < 0.05$ vs. apomorphine) and 70% reinitiated copulation after ejaculation ($P < 0.001$ vs. vehicle, $P < 0.002$ vs. apomorphine and $P < 0.02$ vs. yohimbine).

The comparison of the specific sexual behaviour parameters shown by exhausted rats after an effective dose of yohimbine (2000 μg/kg) with those exhibited after the combined treatment with subthreshold doses of yohimbine (500 μg/kg) and apomorphine (50 μg/kg) revealed no statistically significant differences in any of the measures (Table 1).

3.4. Spontaneous ambulation

The data regarding the effects of the different pharmacological treatments on spontaneous ambulatory behaviour are presented in Tables 2 and 3. As it can be seen in Table 2, a significant decrease in the mean counts was found only after the intermediate dose of apomorphine (100 μg/kg) when compared to its proper vehicle control. Although statistical comparison of spontaneous ambulation after haloperidol treatment failed to reach significance as compared to vehicle treated rats, a diminution was observed in the group receiving the highest dose (250 μg/kg). Some of the animals in this group showed some degree of motor impairment (circling behaviour) that interfered with copulation.

Table 3 shows that after both combined treatments a significant diminution in spontaneous ambulation was found as compared with control groups. However, when analysing the subjects' behaviour individually, no relationship between a reduced number of counts and the ability to

Table 2
Spontaneous ambulatory behaviour after single treatments

Treatment (μg/kg)	*n*	Counts/10 min (Mean ± S.E.)
Vehicle 1	10	367.4 ± 22.7
Yohimbine 500	7	353.7 ± 26.0
Yohimbine 1000	8	286.6 ± 40.5
Yohimbine 2000	8	304.3 ± 34.1
Vehicle 2	8	322.1 ± 28.0
Haloperidol 125	8	270.4 ± 50.0
Haloperidol 250	8	173.6 ± 47.7
Vehicle 3	8	313.4 ± 19.6
Apomorphine 50	8	259.3 ± 17.4
Apomorphine 100	8	205.4 ± 20.9[a]
Apomorphine 200	8	287.8 ± 24.8

[a] $P < 0.05$ vs. vehicle 3, Dunnet's *t*-test.

Table 3
Spontaneous ambulatory behaviour after combined treatments

Treatment (μg/kg)	*n*	Counts/10 min (Mean ± S.E.)
Vehicle 1 + vehicle 2	18	347.3 ± 18.0
Yohimbine 2000 + haloperidol 125	18	213.0 ± 23.3[a]
Vehicle 1 + vehicle 3	18	343.4 ± 16.2
Yohimbine 500 + apomorphine 50	7	234.0 ± 23.8[a]

[a] $P < 0.05$ vs. their respective vehicle control, Dunnet's *t*-test.

copulate and achieve ejaculation was found. Thus, subjects not copulating had control values of spontaneous ambulation while others achieving ejaculation showed a diminished number of counts.

4. Discussion

The present study confirms previous findings showing that both yohimbine (Rodríguez-Manzo and Fernández-Guasti, 1994) and apomorphine (Mas et al., 1995b) are able to induce sexual behaviour expression in sexually satiated rats. A dose–response profile is observed with both treatments in the percentages of exhausted rats showing each of the sexual behaviour responses. Data on motor activity reveal that apomorphine, at the effective dose (200 μg/kg), does not affect spontaneous ambulatory behaviour.

Haloperidol injection, at the dose levels tested, was unable to induce mating behaviour in satiated rats. Although statistical analysis fails to reveal a significant decrease in spontaneous ambulation, motor impairment (circling behaviour) is observed in some animals at the highest dose used (250 μg/kg). The affected animals are unable to copulate. However, animals not showing motor alterations are also unable to copulate. Thus, the inability to show sexual behaviour seems not to rely on unspecific drug effects. Nevertheless, this side effect precludes the testing of higher doses of haloperidol in satiated rats.

The data obtained after the combined treatments reveal that haloperidol, a nonselective dopaminergic antagonist, is able to block the yohimbine-induced sexual behaviour expression in sexually satiated animals. Thus, after the injection of an effective dose of yohimbine (2000 μg/kg) plus a dose of haloperidol not inducing motor disturbances (125 μg/kg), the proportion of satiated rats showing sexual behaviour is not significantly different from that found in the control group. Although this combined treatment reduced spontaneous ambulatory behaviour, the individual analysis of the subjects' behaviour, reveals no relationship between a reduced number of counts and the ability to copulate and achieve ejaculation.

On the other side, the simultaneous injection of subthreshold doses of yohimbine and apomorphine synergised to induce mating behaviour in satiated rats. A diminution in the mean number of counts is found after the combined injection of yohimbine and apomorphine. No relationship could again be established between reduced ambulation and the ability to copulate for a given subject. In further support of this last observation is the fact that the increase in the proportion of copulating subjects is not different from that observed after the injection of an effective dose of yohimbine. Moreover, analysis of the specific sexual behaviour parameters exhibited after either of these treatments show no significant differences in any of the measures. The data obtained with both combined pharmacological treatments suggest that the dopaminergic system might be the ultimate responsible for yohimbine action.

Pharmacological manipulation of sexually exhausted rats has revealed the participation of both, the noradrenergic and the dopaminergic systems in the control of the sexual inhibition that follows copulation to exhaustion. Regarding the noradrenergic system, it has been shown that yohimbine significantly increases the proportion of sexually exhausted rats showing mating behaviour 24 h after the copulation to exhaustion session (Rodríguez-Manzo and Fernández-Guasti, 1994). Additionally it has been demonstrated that the neurotoxic lesion of the noradrenergic system blocks the ability of the 5-HT_{1A} agonist, 8-hydroxi-2-(di-*n*-propylamino)tetralin (8-OH-DPAT), and the μ and δ-opioid receptor antagonist, naloxone, to induce mating behaviour in sexually satiated rats (Rodríguez-Manzo and Fernández-Guasti, 1995b). This last finding suggests that the integrity of the noradrenergic system is essential for the pharmacological re-establishment of copulatory behaviour in sexually exhausted rats.

In relation to the dopaminergic system, neurochemical measurements during copulation to exhaustion, the ensuing sexual refractoriness period and the spontaneous resumption of mating have revealed important changes in dopamine metabolites' levels in the medial preoptic area. (Mas et al., 1995a). In addition, direct measurement of dopamine levels in the nucleus accumbens during copulation to exhaustion and the so called 'Coolidge effect' (the reinitiation of sexual behaviour in sexually satiated animals in response to a novel receptive female) demonstrated changes also in dopamine efflux (Fiorino et al., 1997). Finally, apomorphine, a dopaminergic agonist has been shown to reverse sexual exhaustion (Mas et al., 1995b). Thus, both neurotransmitter systems appear to play a major role in the sexual exhaustion phenomenon. However, as mentioned earlier, two other findings appear difficult to reconcile with the apparent key role played by the noradrenergic system in sexual satiation: on the one side, yohimbine treatment to noradrenaline depleted rats is still able to induce mating behaviour when sexually exhausted (Rodríguez-Manzo and Fernández-Guasti, 1995b) and on the other, the neurotoxic lesion of this neurotransmitter system lacks an effect on the increase in the proportion of copulating satiated rats induced by the 'Coolidge effect' (Rodríguez-Manzo, 1999).

Based on the above mentioned data it appeared conceivable that the dopaminergic system might be the responsible for the yohimbine-induced sexual behaviour expression in satiated rats. The present series of experiments support this notion.

Yohimbine is an indole alkaloid exhibiting a multiplicity of actions. This drug acts both, on the noradrenergic and dopaminergic systems. It increases the turnover of rat cerebral noradrenaline through the interaction with α_2-adrenoceptors (Andén and Strömbom, 1974). The alkaloid

also increases brain dopamine turnover, an effect attributed to an indirect action of the drug on dopaminergic neurones exerted through changes in noradrenaline transmission (Andén and Grabowska, 1976). This same effect of yohimbine has been observed in mice and was proposed to be exerted by the selective blockade of α_2-autoreceptors (Andén et al., 1982). There are other works describing both physical (Maeda et al., 1994; Berridge et al., 1997) and functional (Pycock, 1977; Gresch et al., 1995) links between the noradrenergic and dopaminergic neurotransmitter systems; and others particularly demonstrating actions of α_2-adrenoceptor antagonists on both the noradrenergic and dopaminergic systems (Andén and Grabowska, 1976; Scatton et al., 1980; Johnston and File, 1989; Ferrari and Giuliani, 1993; Xu et al., 1993; Haapalinna et al., 1997).

It has been reported that most of the conditions that activate nucleus accumbens dopaminergic activity do have some degree of motivational significance, including both appetitive and aversive conditions. (Salamone, 1996). The data obtained with both physiological and pharmacological manipulations of the sexual exhaustion state point to an important involvement of sexual motivation in this phenomenon. Thus, during sexual exhaustion development, those sexual behaviour parameters that have been most directly associated to the motivational component of sexual behaviour appear progressively inhibited (Lawrence and Barfield, 1975; Rodríguez-Manzo and Fernández-Guasti, 1994) suggesting a decline in sexual motivation resulting from multiple ejaculation. On the other side, the different pharmacological treatments that restore sexual behaviour expression in satiated rats facilitate these same measures (Rodríguez-Manzo and Fernández-Guasti, 1994, 1995a,b). Finally, a presumed physiological increase in sexual motivation in satiated rats, by means of presenting them to a novel stimulus female (Coolidge effect), blocks the establishment of the sexual inhibition that characterises sexual exhaustion (Rodríguez-Manzo, 1999). Altogether, these data support the notion of the motivational component of sexual behaviour playing a key role in the sexual satiation phenomenon.

Both, the noradrenergic and the dopaminergic systems have been implicated in sexual motivation (Clark et al., 1984, 1985; Smith et al., 1987; Scaletta and Hull, 1990; Benelli et al., 1993; Mitchell and Gratton, 1994; Hull et al., 1995, 1997; Van Furth et al., 1995). Thus, an interaction between these two transmitter systems in the regulation of the motivational component of this behaviour is plausible.

Le Moal (1995) declares that the dopaminergic system plays a general role in activation and that a functional concept of the dopaminergic system is to activate the final common pathway of several integrative processes. Present data support this notion by suggesting that the dopaminergic system might be the final common pathway for the induction of mating behaviour in sexually satiated rats.

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