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Serotonin and sexual behavior in the male rabbit

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Summary. Sexual behavior was evaluated in sexually experienced male rabbits after the administration of different serotonergic drugs. The serotonin$_{1A}$ receptor agonist 8-OH-DPAT, 1 mg/kg, inhibited male rabbit sexual behavior when animals were tested 15 min after subcutaneous (SC) administration of this compound. Lower doses, 0.25 and 0.5 mg/kg, were ineffective at a test 30 min after drug injection. Furthermore, 8-OH-DPAT, 0.25 mg/kg, failed to revert the inhibitory effects upon sexual behavior produced by lidocaine application to the rabbit penis. Stimulation of 5-HT$_{1B/2C}$ receptors by TFMPP, at doses between 0.625 and 2.5 mg/kg, produced a drastic inhibition of sexual behavior when the drug was administered SC 30 min before behavioral observation. Doses below 5 mg/kg were ineffective when given intraperitoneally 15 min before test. When the 5-HT$_{1D/2C}$ receptors were stimulated by the agonist mCPP a reduced number of mounts and ejaculations was observed after the SC administration of 1.25 and 2.5 mg/kg. Similarly, the mixed 5-HT agonist/antagonist lisuride reduced the percentage of rabbits displaying mounting behavior at doses of 0.25 and 0.5 mg/kg SC. All compounds tested produced a clear inhibition of male rabbit sexual behavior independently of the receptor subtype activated. These results are at variance with previous observations in rats where 8-OH-DPAT and lisuride produced a drastic facilitation of masculine coital behavior. Moreover, while the inhibition of male sexual behavior in rats produced by TFMPP and mCPP is associated with a disruption of the execution of this behavior, in rabbits these compounds reduced sexual motivation. These results indicate that the effects of serotonergic drugs on sexual behavior are species specific.

Keywords: Rabbit, serotonin, sexual behavior, penile anesthesia.

Introduction

It is well established that serotonin (5-HT) neurones participate in the control of sexual behavior in the rat. The behavioral effects depend on the receptor subtype activated (Fernández-Guasti et al., 1989, 1992; Ahlenius and Larsson, 1997, 1998). The stimulation of the 5-HT_{1A} receptor facilitates sexual behavior in male rats. A reduction in the number of preejaculatory intromissions and in the ejaculation latency is observed (Andersson and Larsson, 1994; Arnone et al., 1995; Mos et al., 1991; Rehman et al., 1999). The most dramatic facilitation produced by 5-HT_{1A} receptor agonists is observed after administration of 8-hydroxy-2(di-n-propylamino)tetralin (8-OH-DPAT). Some rats ejaculate after only one intromission (Ahlenius and Larsson, 1987; Ahlenius et al., 1981). Animals with low levels of sexual activity, induced by castration, showed a facilitation of coital behavior after administration of this compound (Ahlenius and Larsson, 1987; Ahlenius et al., 1981). Moreover, the behavioral effects of section of the dorsal penile nerve, i.e. increased number of mounts and reduced number of intromissions and ejaculations, were completely reversed by 8-OH-DPAT (Dahlöf et al., 1988). By contrast, stimulation of 5-$HT_{1B/2C}$ receptors by 1-(m-trifluoromethylphenyl)piperazine (TFMPP) inhibited male rat sexual behavior as evidenced by an increase in the number of mounts and intromissions and a prolonged ejaculation latency (Fernández-Guasti and Rodríguez-Manzo, 1992; Fernández-Guasti et al., 1989; Mendelson and Gorzalka, 1990). The behavioral actions of 8-OH-DPAT and TFMPP on male rat sexual behavior appear to be independent of the route of administration since similar effects were described after intrathecal (Lee et al., 1990) intracerebral (Fernández-Guasti et al., 1992) or systemic (Ahlenius et al., 1981; Fernández-Guasti and Rodríguez-Manzo, 1992; Mendelson and Gorzalka, 1990) injection.

Few studies have evaluated the effects of drugs that influence 5-HT neurotransmission on male sexual behavior in other species. The administration of the 5-$HT_{1D/2C}$ receptor agonist, m-chlorophenylpiperazine (mCPP) to male rhesus monkeys facilitated the occurrence of penile erections (Pomerantz et al., 1993a; Szele et al., 1988) but produced an inhibition of sexual behavior by lengthening the ejaculation latency (Pomerantz et al., 1993b) and reducing the percentage of animals initiating and achieving ejaculation (Pomerantz et al., 1993a). The effects of stimulating 5-HT_{1A} receptors with 8-OH-DPAT have been studied in non-human primates and ferrets. The administration of this compound had no effect on penile erections in rhesus monkeys when tested alone (Pomerantz et al., 1993a; Szele et al., 1988), but decreased the percentage of monkeys exhibiting penile erections when the female was present (Pomerantz et al., 1993a). While very low doses of 8-OH-DPAT (5 or 10 μg/kg) facilitated sexual behavior in monkeys, higher doses that facilitate sexual behavior in rats (0.1 and 1 mg/kg; Ahlenius and Larsson, 1987) lengthened the monkeys' ejaculation latency (Pomerantz et al., 1993b). A similar inhibition of sexual behavior was observed in male ferrets (Paredes et al., 1994). It thus appears that 8-OH-DPAT exerts species-specific actions on the expression of sexual behavior facilitating masculine sexual behavior in rats

and (at very low doses) in rhesus monkeys whereas it inhibits this behavior in the ferret.

In the present study the effects of 8-OH-DPAT (5-HT_{1A} agonist), TFMPP (5-$HT_{1B/2C}$ agonist), mCPP (5-$HT_{1D/2C}$ agonist) and lisuride (mixed 5-HT agonist/antagonist), a drug with effects very similar to those of 8-OH-DPAT (Ahlenius et al., 1980), upon male rabbit sexual behavior were evaluated with the purpose of comparing the effects in this species with those previously reported in others. Although TFMPP, mCPP and lisuride are not the most specific agonists available, we preferred to employ these drugs rather than more recent agonists with higher receptor selectivity because data from several species are available for the former but not for the latter. In an additional experiment, a group of rabbits had their penis desensitized by lidocaine and were then treated with 8-OH-DPAT. The behavioral effects of desensitisation of the penis (increased number of mounts and reduced number of intromissions) are similar in rats (Adler and Bermant, 1966; Contreras and Ågmo, 1993), cats (Aronson and Cooper, 1968), monkeys (Herbert, 1973) and rabbits (Ågmo, 1976). Since 8-OH-DPAT blocks these effects in rats (Dahlöf et al., 1988) it was considered of interest to evaluate whether this also occurs in the rabbit. These studies would allow us to determine if the serotonergic control of sexual behavior in rabbits is similar to that in rodents, carnivores and primates.

Materials and methods

Subjects

Male New Zealand White rabbits (3–4 kg) purchased from Bioterio México (Mexico City) received tap water and food (Albamex rabbit pellets) ad libitum. They were housed in individual stainless steel cages (45 × 45 × 30 cm high) under a natural light/dark cycle at a room temperature of 22–24°C. Females were ovariectomized at least 2 weeks before use under pentobarbital anesthesia (40 mg/kg). Receptivity was induced by SC injections, once weekly, of 2.5 mg estradiol valerianate (Schering Mexicana, Mexico City) in 0.25 ml corn oil. This treatment maintained constant receptivity for about 3–4 months (Ågmo et al., 1996; Paredes et al., 1998).

The experiments reported herein were performed according to the guidelines for the care and use of laboratory animals established and promulgated by the National Institutes of Health of the United States of America and in agreement with applicable local laws.

Behavioral testing

Males that ejaculated at least once in three screening tests were used in the experiment. The males were placed in an observation cage (thick wire mesh, 100 × 50 × 40 cm high) 5 min before the introduction of a receptive female. Coital tests were performed at least 48 hrs apart and the following parameters were recorded: Mount latency, time from introduction of the female until the first mount with pelvic thrusting; ejaculation latency, time from introduction of the female until the first ejaculation (the rabbit ejaculates upon every vaginal penetration); postejaculatory interval, time from one ejaculation until the next mount; number of mounts with pelvic thrusting and the number of ejaculations. Tests lasted 10 min. If an animal was in postejaculatory interval at that time the test was continued until the following mount or until the interval exceeded 10 min.

Drugs

The specific 5-HT_{1A} receptor agonist 8-OH-DPAT (±-2-dipropylamino-8-hydroxy-1,2,3,4,-tetrahydronaphtalene HBr), the 5-$HT_{1B/2C}$ agonist TFMPP (N-(3-trifluoromethylphenyl)piperazine HCl) (both from Research Biochemicals Inc, Natick, MA), the 5-$HT_{1D/2C}$ receptor agonist mCPP (m-chlorophenylpiperazine HCl) (Sigma Chemical Co., St. Louis, MO) and the mixed 5-HT agonist/antagonist lisuride (R(+)-N^1-[(8α)-9,10-didehydro-6-methylergolin-8-yl]-N,N-diethylurea hydrogen maleate) (Schering AG, Berlin) were dissolved in saline and injected SC or intraperitoneally (IP) in a volume of 1 ml/kg. All doses mentioned refer to the form of the compounds indicated above.

The following intervals were used between drug administration and behavioral observation: 8-OH-DPAT, 15 or 30 min; TFMPP, 15 min; mCPP, 30 min; lisuride, 15 min. All subjects were given all doses of a given drug in counterbalanced order. Whenever possible an equal number of subjects received the different doses of a given drug at a particular experimental session. There was an interval of at least 48 hrs between successive drug treatments. In one group of animals treated with 8-OH-DPAT (0.25 mg/kg) lidocaine (Xylocain® paste, 5%, Astra, Södertälje, Sweden) was applied to the penis immediately before testing. The penile sheath was manually retracted and the penis gently rubbed with lidocaine for about 1 min with the male placed in a supine position. In the control treatment rabbits were treated in exactly the same way but Vaseline paste was applied to the penis.

Statistical analysis

The proportion of subjects displaying mount and ejaculation was evaluated with Cochran's Q test or McNemar's test for the significance of changes when only two treatments were compared. The number of mounts and ejaculations were evaluated with Friedman's two-way ANOVA. In case of significance (or when two treatments were compared) the Wilcoxon T test was used. Data from all animals were included in this analysis. Mount and ejaculation latencies as well as the postejaculatory interval were analyzed with the one-way Kruskal-Wallis ANOVA and/or the Mann-Whitney U-test when appropriate. Here, only data from animals that displayed sexual behavior was used. A sexually inactive animal has, obviously, no latency. This means that the number of subjects from which data were obtained differed between doses, precluding the use of statistical tests for repeated measures. Parametric tests could not be employed because of non-homogenous error variances as determined by Hartley's F_{max} test. Probabilities are two tailed.

Results

No statistically significant effect was obtained on the latencies or on the postejaculatory interval. These data are, therefore, neither shown in the tables nor discussed in the text.

The administration of 8-OH-DPAT, 1 mg/kg, produced a significant inhibition of male rabbit sexual behavior when the animals were tested 15 min postinjection. As can be seen in Table 1, the percentage of males displaying mounts and ejaculations as well as the number of mounts and ejaculations during the test were significantly reduced. One possible explanation for the inhibitory effect could be that the drug had other behavioral actions (the 5-HT syndrome) that were incompatible with the execution of sexual behavior. We therefore performed an additional experiment where the doses were lower and the interval between drug injection and test was longer. It was, in fact,

Table 1. Sexual behavior in male rabbits injected with 8-OH-DPAT either 15 or 30 minutes before behavioral observation. Doses are expressed in mg/kg

	15 min before (N = 8)		30 min before (N = 12)		
	NaCl	1	NaCl	0.25	0.50
Mount %	100	38*	75	67	50
Ejaculation %	100	25**	75	50	50
Number of mounts	3.8 ± 0.8	1.3 ± 0.6*	3.6 ± 0.9	2.1 ± 0.7	2.0 ± 0.7
Number of ejaculation	3.0 ± 0.4	0.8 ± 0.5**	1.9 ± 0.4	1.3 ± 0.5	1.2 ± 0.4

Data are mean ± s.e.m. *Different from saline, $p < 0.05$; **$p < 0.01$

increased to 30 min. In the rat, brain concentration of 8-OH-DPAT peaks about 15 min after SC administration and remains high at 30 min although the 5-HT syndrome then has disappeared (Yu and Lewander, 1997). It is not certain that the time course is identical in rabbits, but it can at least be expected to show some similarity. The additional experiment showed that 8-OH-DPAT, 0.25 or 0.5 mg/kg, lacked significant effect on sex behavior (Table 1).

The application of lidocaine to the rabbit penis produced a significant reduction of the proportion of animals displaying ejaculation as well as a reduced number of ejaculations during the test. As expected, the number of mounts increased after penile anesthesia. The administration of 8-OH-DPAT, 0.25 mg/kg, was unable to reduce the inhibitory effects produced by lidocaine application. As can be seen in Table 2, none of the animals treated with lidocaine plus 8-OH-DPAT ejaculated.

The stimulation of 5-$HT_{1B/2C}$ receptors with TFMPP had effects only at large doses when the compound was given IP. The number of mounts and ejaculations were significantly reduced after 5 and 10 mg/kg respectively whereas lower doses were completely ineffective (see Table 3). However, a drastic inhibition of sexual behavior was observed 30 min after SC administration of TFMPP. As can be seen in Table 4, the percentage of animals display-

Table 2. Sexual behavior in male rabbits after application of lidocaine in animals previously injected with 0.25 mg/kg of 8-OH-DPAT. N = 12

	NaCl + vaseline	NaCl + lidocaine	Lidocaine + 8-OH-DPAT
Mount %	100	75	75
Ejaculation %	100	25*	0**
Number of mounts	3.3 + 0.5	7.6 ± 1.7*	6.8 ± 2.7
Number of ejaculations	2.1 ± 0.6	0.3 ± 0.1**	0.0 ± 0.0**

Data are mean ± s.e.m. *Different from saline, $p < 0.05$; **$p < 0.01$

Table 3. Sexual behavior in male rabbits 15 min after intraperitoneal injection of TFMPP. Doses are expressed in mg/kg. N = 12

	NaCl[a]	0.25	0.50	1	5	10
Mount %	100	83	92	75	75	58
Ejaculation %	100	75	83	58	75	58
Number of mounts	4.2 ± 0.8	3.4 ± 0.6	4.0 ± 0.6	4.5 ± 1.0	2.7 ± 0.6*	4.3 ± 1.3
Number of ejaculations	2.5 ± 0.3	2.2 ± 0.5	1.8 ± 0.4	1.5 ± 0.4	2.2 ± 0.4	0.4 ± 0.4*

[a] Two independent groups of animals were used in this experiment (one for NaCl, 0.25 and 0.5 mg/kg and another for NaCl, 1, 5 and 10 mg/kg). The saline treated groups did not differ significantly on any parameter. Therefore they were pooled for presentation. Statistical comparisons were always made between the different doses of TFMPP and the respective control. Data are mean ± s.e.m. * Different from saline, $p < 0.05$

Table 4. Sexual behavior in male rabbits 30 min after subcutaneous injection of TFMPP. Doses are expressed in mg/kg. N = 12

	NaCl	0.625	1.25	2.5
Mount %	100	66	50*	25**
Ejaculation %	100	66*	66*	50**
Number of mounts	3.0 ± 0.3	1.7 ± 0.4*	0.9 ± 0.3**	0.7 ± 0.4**
Number of ejaculations	2.4 ± 0.3	1.2 ± 0.4**	0.9 ± 0.3**	0.6 ± 0.4**

Data are mean ± s.e.m. * Different from saline, $p < 0.05$; ** $p < 0.01$

Table 5. Sexual behavior in male rabbits 30 min after subcutaneous injection of mCPP. Doses are expressed in mg/kg. N = 7

	NaCl	0.625	1.25	2.5
Mount %	100	86	57	43
Ejaculation %	100	86	57	29
Number of mounts	3.1 ± 0.2	2.3 ± 0.6	1.1 ± 0.5*	1.1 ± 0.6*
Number of ejaculations	2.6 ± 0.4	2.1 ± 0.5	1.1 ± 0.5*	0.6 ± 0.4*

Data are mean ± s.e.m. * Different from saline, $p < 0.05$

ing mounts and ejaculations as well as the number of mounts and ejaculations during the test were reduced at all doses tested.

A reduction of the number of mounts and ejaculations was also observed when the 5-$HT_{1D/2C}$ receptors were stimulated by administration of mCPP (see Table 5). Similarly, the mixed 5-HT agonist/antagonist lisuride significantly reduced the percentage of rabbits displaying mounting behavior as well as the number of mounts during the test (see Table 6).

Table 6. Sexual behavior in male rabbits 15 min after treatment with lisuride. Doses are expressed in mg/kg. N = 12

	NaCl	0.125	0.25	0.5
Mount %	92	67	42*	25**
Ejaculation %	67	50	42	25
Number of mounts	4.7 ± 1.1	3.8 ± 1.2	1.3 ± 0.5**	0.6 ± 0.4**
Number of ejaculations	1.6 ± 0.5	1.0 ± 0.4	0.9 ± 0.3	0.6 ± 0.3

Data are mean ± s.e.m. *Different from saline, $p < 0.05$; **$p < 0.01$

Discussion

With regard to effect on sexual behavior, the only clear distinction that can be made between serotonin receptor subtypes is that between a stimulatory effect of 5-HT_{1A} and an inhibitory effect of 5-HT_{1B} and probably also 5-HT_{2C} receptors (Klint et al., 1992). The opposite effects of 5-HT_1 receptor subtypes was first established using the same drugs as the ones used in the present study (Fernández-Guasti et al., 1989), and has thereafter been confirmed using more selective drugs (e.g. Ahlenius and Larsson, 1998). It seems, then, that for the purpose of analyses of drug effects on sexual behavior TFMPP and mCPP can be considered as 5-HT_{1B} agonists while 8-OH-DPAT can be considered a 5-HT_{1A} agonist. This does not mean that all their behavioral effects can be attributed to these receptors, but the most evident effects on sexual behavior can be so. It must be observed that the studies mentioned above have all been performed on rats. Nevertheless, the drugs employed should have been able to reveal any opposing effects of 5-HT_{1A} and 5-$HT_{1B/2C}$ receptors, if such effects existed.

All compounds tested produced a clear inhibition of male rabbit sexual behavior independently of the receptor subtype they activate. It must be noted that efforts were made to administer 8-OH-DPAT in such a way as to maximize the possibility to observe facilitatory effects (low doses, long interval injection – test, hence low incidence of the 5-HT syndrome). Despite this, no facilitation of sex behavior was obtained. Furthermore, lisuride, another drug with facilitatory effects in rats, also produced a dose-dependent inhibition of male rabbit sexual behavior. There is not much reason to believe that the inhibitory effects observed here are secondary to drug-induced motor disturbances. It should be noted that 8-OH-DPAT as well as lisuride stimulate sex behavior in rats even at doses where motor effects and other components of the 5-HT syndrome can be expected to be intense (Ahlenius and Larsson, 1987; Da Prada et al., 1977). Moreover, we have previously reported that rabbits are more resistant to motor effects of several kinds of drugs than rats are (Ågmo and Fernández, 1989; Ågmo et al., 1996; Paredes et al., 1998). It seems most unlikely, then, that motor actions can account for the consistent inhibitory effects of the several serotonin$_1$ receptor agonists employed.

The effects of 8-OH-DPAT found in the present study are at variance with what is observed in male rats and monkeys (see Introduction). It is evident

that the effects reported in rats and monkeys (reduced number of preejaculatory intromissions and/or shortened ejaculation latency) cannot be exactly replicated in rabbits, because rabbits ejaculate upon every intromission. There is, then, no possibility to reduce the number of preejaculatory intromissions. Furthermore, ejaculation latency as it is normally defined in rats (time from the first intromission until ejaculation) does not exist in rabbits. Nevertheless, in addition to its facilitatory effects on ejaculation 8-OH-DPAT has motivational effects in rats. This is made evident by the fact that the drug increases male-to-male mounting (Da Prada et al., 1977) and facilitates sex behavior in castrates (Ahlenius and Larsson, 1987; Ahlenius et al., 1981). No facilitatory effect on motivation was observed in the rabbit. For example, there was no reduction of mount latency.

Despite the fact that the pattern of sexual behavior varies across species, some experimental manipulations produce consistent effects in several species. One such manipulation is, as was mentioned in the Introduction, the effects of penile anesthesia. In fact, the behavioral effects of reduced penile sensitivity are remarkably similar in rats and rabbits (Ågmo, 1976; Contreras and Ågmo, 1993). 8-OH-DPAT normalizes sexual behavior in rats with reduced penile sensitivity (Dahlöl et al., 1988), and it could be expected that the drug would have a similar effect also in the rabbit. This was not the case, however. The dose we used is the same that was successfully employed in the Dahlöf et al. (1988) study. Obviously, it can be argued that other doses might have been effective in the rabbit. However, a large dose of this drug is inhibitory by itself and could, therefore, not be used. There is no compelling reason to believe that lower doses would have been effective, but this possibility cannot be entirely ruled out. The fact that Dahlöf et al. (1988) used transsection of the dorsal penile nerve while we used lidocaine to reduce penile sensitivity does not seem to be of any fundamental importance. In the rat, the behavioral consequences of these two treatments are very similar (Contreras and Ågmo, 1993). It seems safe to conclude that stimulation of 5-HT1_A receptors have different effects in rats and rabbits.

Inhibition of male sexual behavior after 8-OH-DPAT administration has also been observed in ferrets (Paredes et al., 1994). The male ferret grips the female on the dorsal surface of the neck, mounts her and begins pelvic thrusting until intromission is achieved. Doses that facilitate sex behavior in male rats produced a drastic inhibition of neck gripping, and hence of male coital behavior in ferrets while lower doses had no effect (Paredes et al., 1994).

The stimulation of 5-HT$_{1B/2C}$ and 5-HT$_{1D/2C}$ receptors by the administration of TFMPP and mCPP, respectively, also inhibited male rabbit sex behavior. The effects of TFMPP are more dramatic after SC than after IP injection. A similar difference in magnitude of effect according to the route of administration was described for morphine and naloxone (Ågmo et al., 1994) as well as for the GABA agonists THIP and baclofen (Paredes et al., 1998). In all cases the SC injections were more effective. At present little information is available concerning species differences in metabolic clearance after different

routes of administration of these compounds. Only pharmacokinetic studies could provide answer to these questions.

Although TFMPP and mCPP produce an inhibition of male sexual behavior in both rats and rabbits, the inhibitory effects appear to be related to different aspects of the mating pattern. In rats these compounds increased the number of mounts without affecting the percentage of animals displaying this behavior. They also produced a drastic reduction of the percentage of animals displaying intromissions and ejaculations and prolonged the ejaculation latency (Fernández-Guasti et al., 1989; Mendelson and Gorzalka, 1990). However, in rabbits they reduced the *proportion* of animals displaying mounts and ejaculations as well as the *number* of mounts and ejaculations during the test. It appears then, that in the rat the stimulation of 5-$HT_{1B/2C}$ and 5-$HT_{1D/2C}$ receptors has no effect on sexual motivation (no change was observed in mount latency and percentage of animals displaying mounts) but they disrupt the execution of the behavior once it is initiated (reduced percentage of animals displaying ejaculation and prolonged ejaculation latency). At contrast, in the rabbit the stimulation of 5-$HT_{1B/2C}$ and 5-$HT_{1D/2C}$ receptors appeared to reduce both sexual motivation and performance of sexual acts.

It is interesting to observe that rats and rhesus monkeys (Michael and Saayman, 1967) require several preejaculatory intromissions while the rabbit and ferret (Miller and Anderson, 1989) typically ejaculate after a single mount with intromission. In the former animals 8-OH-DPAT has a facilitatory action while it is inhibitory in the latter. It is possible, then, that the effects of manipulations of 5-HT_{1A} receptors on sexual behavior depend on whether the species require several intromissions to ejaculate or if the male ejaculates after a single intromission. More comparative studies are needed to further test this hypothesis.

The present studies do not give any information concerning neither the mode nor the site of action of the drugs employed. This, however, was not the purpose of them. Moreover, systemic drug injections are not the most adequate way of obtaining such information. On the other hand, most drugs employed clinically are administered systemically. Among the common side effects of clinical use of drugs facilitating serotonergic neurotransmission are reduced sexual functions, including diminished arousal, delayed ejaculation and absence of orgasm (Herman et al., 1990; Lane, 1997). It seems, then, that humans, rats, and rabbits are similar in their response to generally facilitated serotonergic activity. The stimulatory effects of 5-HT_{1A} agonists found in rats have not been reported for humans using this kind of drugs. Although the literature is not abundant, one study with buspirone did not find any evidence for hypersexuality (Othmer and Othmer, 1987).

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References

Adler N, Bermant G (1966) Sexual behavior of male rats: effects of reduced sensory feedback. J Comp Physiol Psychol 61: 240–243

Ågmo A (1976) Mating in male rabbits after anesthesia of the glans penis. Physiol Behav 17: 435–437

Ågmo A, Fernández H (1989) Dopamine and sexual behavior in the male rat: a re-evaluation. J Neural Transm 77: 21–37

Ågmo A, Paredes RG, Contreras JL (1994) Opioids and sexual behavior in the male rabbit: the role of central and peripheral opioid receptors. J Neural Transm 97: 211–223

Ågmo A, Paredes RG, Ramos I, Contreras JL (1996) Dopamine and sexual behavior in the male rabbit. Pharmacol Biochem Behav 55: 289–295

Ahlenius S, Larsson K (1987) Evidence for a unique pharmacological profile of 8-OH-DPAT by evaluation of its effects on male rat sexual behavior. In: Dourish CT, Ahlenius S, Hutson PH (eds) Brain 5-HT_{1A} receptors: behavioral and neurochemical pharmacology. Ellis Horwood, Chichester, pp 185–198

Ahlenius S, Larsson K (1997) Specific involvement of central 5-$HT1_A$ receptors in the mediation of male rat ejaculatory behavior. Neurochem Res 22: 1065–1070

Ahlenius S, Larsson K (1998) Evidence for an involvement of 5-$HT1_B$ receptors in the inhibition of male rat ejaculatory behavior produced by 5-HTP. Psychopharmacology 137: 374–382

Ahlenius S, Larsson K, Svensson L (1980) Stimulating effects of lisuride on masculine sexual behavior of rats. Eur J Pharmacol 64: 47–51

Ahlenius S, Larsson, Svensson L, Hjorth S, Carlsson A, Lindberg P, Wikström H, Sanchez D, Arvidsson LE, Hacksell U, Nilsson JLG (1981) Effects of a new type of 5-HT receptor agonist on male rat sexual behavior. Pharmacol Biochem Behav 15: 785–792

Andersson L, Larsson K (1994) Effects of FG 5893, a new compound with 5-HT_{1A} receptor agonistic and 5-HT_2 receptor antagonistic properties, on male rat sexual behavior. Eur J Pharmacol 255: 131–137

Arnone M, Baroni M, Gai J, Guzzi U, Desclaux MF, Keane PE, Le Fur G, Soubrié P (1995) Effect of SR 59026A, a new 5-HT_{1A} receptor agonist, on sexual activity in male rats. Behav Pharmacol 6: 276–282

Aronson LR, Cooper ML (1968) Desensitization of the glans penis and sexual behavior in cats. In: Diamond M (ed) Perspectives in reproduction and sexual behavior. Indiana University Press, Bloomington, pp 51–82

Contreras JL, Ågmo A (1993) Sensory control of the male rat's copulatory thrusting patterns. Behav Neural Biol 60: 234–240

Dahlöf LG, Ahlenius S, Larsson K (1988) Copulatory performance of penile desensitized male rats following the administration of 8-OH-DPAT. Physiol Behav 43: 841–843

Da Prada M, Bonetti EP, Keller HH (1977) Induction of mounting behavior in female and male rats by lisuride. Neurosci Lett 6: 349–353

Fernández-Guasti A, Rodríguez-Manzo G (1992) Further evidence showing that the inhibitory action of serotonin on rat mascukine sexual behaviour is mediated after the stimulation of 5-HT_{1B} receptors. Pharmacol Biochem Behav 42: 529–533

Fernández-Guasti A, Escalante AL, Ågmo A (1989) Inhibitory actions of various $5HT_{1B}$ receptor agonists on rat masculine sexual behavior. Pharmacol Biochem Behav 34: 811–816

Fernández-Guasti A, Escalante AL, Ahlenius S, Hillegaart V, Larsson K (1992) Stimulation of 5-HT_{1A} and 5-HT_{1B} receptors in brain regions and its effects on male rat sexual behaviour. Eur J Pharmacol 210: 121–129

Herbert J (1973) The role of the dorsal penile nerves of the penis in the sexual behavior of the male rhesus monkey. Physiol Behav 10: 293–300

Herman JB, Brotman AW, Pollack MH, Falk WE, Biederman G, Rosenbaum GF (1990) Fluoxetine-induced sexual disfunction. J Clin Psychiatry 51: 25–27

Klint T, DahlgrenIL, Larsson K (1992) The selective 5-HT_2 receptor antagonist amperozide attenuates 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane-induced inhibition of male rat sexual behavior. Eur J Pharmacol 212: 241–246

Lane RM (1997) A critical review of selective serotonin reuptake inhibitor-related sexual dysfunction: incidence, possible etiology and implications of management. J Psychopharmacol 11: 72–82

Lee RL, Smith ER, Mas M, Davidson JM (1990) Effects of intrathecal administration of 8-OH-DPAT on genital reflexes and mating behavior in male rats. Physiol Behav 47: 665–669

Mendelson SD, Gorzalka BB (1990) Sex differences in the effects of 1-(m-trifluoromethylphenyl)piperazine and 1-(m-chlophenyl)piperazine on copulatory behavior in the rat. Neuropharmacology 29: 783–786

Michael RP, Saayman GS (1967) Individual differences in the sexual behaviour of male rhesus monkeys (Macaca mulatta) under laboratory conditions. Anim Behav 15: 460–466

Miller BJ, Anderson SH (1989) Failure of fertilization following abbreviated copulation in the ferret (Mustela putorius furo). J Exp Zool 249: 85–89

Mos J, Van Logten J, Bloetjes K, Olivier B (1991) The effects of idazoxan and 8-OH-DPAT on sexual behavior and associated ultrasonic vocalizations in the rat. Neurosci Biobehav Rev 15: 505–510

Othmer E, Othmer SC (1987) Effect of buspirone on sexual function in patients with generalized anxiety disorder. J Clin Psychiatry 48: 201–203

Paredes RG, Kica E, Baum MJ (1994) Differential effects of the serotonin$_{1A}$ agonist, 8-OH-DPAT, on masculine and feminine sexual behavior of the ferret. Psychopharmacology 114: 591–596

Paredes RG, Contreras JL, Ågmo A (1998) GABAergic drugs and sexual behavior in the rabbit: evidence for species-specific effects. J Psychopharmacol 12: 186–191

Pomerantz SM, Hepner BC, Wertz JM (1993a) 5-HT_{1A} and 5-$HT_{1C/1D}$ receptor agonists produce reciprocal effects on male sexual behavior of rhesus monkeys. Eur J Pharmacol 243: 227–234

Pomerantz SM, Hepner BC, Wertz JM (1993b) Serotonergic influences on male sexual behavior of rhesus monkeys: effects of serotonin agonists. Psychopharmacology 111: 47–54

Rehman J, Kayman A, Christ G, Valcic M, Maayani S, Melman A (1999) Modification of sexual behavior of Long-Evans male rats by drugs acting on the 5-HT_{1A} receptor. Brain Res 821: 414–425

Szele FG, Murphy DL, Garrick NA (1988) Effects of fenfluramine, m-chlorophenypiperazine and other serotonin-related agonist and antagonist on penile erections in non-human primates. Life Sci 43: 1297–1303

Yu H, Lewander T (1997) Pharmacokinetic and pharmacodynamic studies of (R)-8-hydroxy-2-(di-n-propylamino)tetralin in the rat. Eur Neuropsychopharmacol 7: 165–172

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