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Effects of a New Type of 5-HT Receptor Agonist on Male Rat Sexual Behavior

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AHLENIUS, S., K. LARSSON, L. SVENSSON, S. HJORTH, A. CARLSSON, P. LINDBERG, H. WIKSTRÖM, D. SANCHEZ, L.-E. ARVIDSSON, U. HACKSELL AND J. L. G. NILSSON. *Effects of a new type of 5-HT receptor agonist on male rat sexual behavior.* PHARMAC. BIOCHEM. BEHAV. 15(5) 785–792, 1981.—8-Methoxy-2-(di-n-propylamino) tetralin (8-OMe-DPAT) and 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT) are two new drugs exerting selective actions on brain 5-HT neurotransmission. In the present experiments we have investigated the effects of these two drugs on male rat sexual behavior. It was found that both drugs reduce the number of intromissions preceding ejaculation and shorten the ejaculation latency. These effects are extremely pronounced and several animals ejaculate at the first intromission. In addition 8-OH-DPAT produced a slight reduction of the post-ejaculatory interval. There were no significant effects on latency to initiate copulation or in the number of mounts preceding ejaculation. Finally, sexual behavior was partly or completely restored in castrated male rats after injection with 8-OMe-DPAT or 8-OH-DPAT.

Male rat Sexual behavior 5-Hydroxytryptamine Catecholamines 8-OMe-DPAT 8-OH-DPAT

CONSIDERABLE evidence indicate that central monoamines are involved in the regulation of male rat sexual behavior. Thus, treatment with *para*-chlorophenylalanine (PCPA), an inhibitor of the 5-hydroxytryptamine (5-HT) synthesis [24], produces a shortening of the ejaculation latency [2,36] and may induce full sexual behavior in rats rendered sexually inactive by castration [39]. An increase in central 5-HT concentration produced by treatment with 5-hydroxytryptophan (5-HTP) and the inhibitor of peripheral aromatic *L*-amino acid decarboxylase benserazide [10], results in a prolongation of the ejaculation latency without affecting the number of ejaculating animals [3] and, with increasing dose, decrease the number of copulating animals [3,26]. The effects produced by 5-HTP and benserazide are enhanced by pretreatment with selective inhibitors of neuronal 5-HT reuptake [4].

Drugs like apomorphine, *L*-DOPA and *d*-amphetamine, which enhance central catecholamine neurotransmission [7], produce a shortening of the ejaculation latency [12, 13, 16], whereas a depletion of central monoamines by treatment with tetrabenazine, which inhibits the granular uptake-storage of monoamines [34], has been shown to impair the display of male rat sexual behavior [13]. The effects on sexual behavior produced by interference with central catecholamine neurotransmission are weaker than corresponding changes produced by interference with central 5-HT neurotransmission. Furthermore, there are no reports showing an activation of copulatory behavior in castrated male rats by treatment with selective catecholamine agonists, as seen after treatment with PCPA or lisuride. It is possible, however, that more specific effects by catecholamine agonists or antagonists are overshadowed by their general actions as central stimulants (e.g., [7]) and depressants (e.g., [1]), respectively.

Recently a new series of drugs with demonstrated ability to affect central 5-HT neurotransmission have been developed in our laboratories. The drugs seem to be directly acting 5-HT receptor agonists [8, 9, 21, 40]. This is indicated by their marked and selective decrease in 5-HTP formation in the limbic forebrain, the corpus striatum and in the hemispheres after inhibition of aromatic *L*-amino acid decarboxylase by means of 3-hydroxybenzylhydrazine (NSD-1015) in rats pretreated with reserpine (for experimental details see [41]) and by the appearance of a behavioral syndrome characteristic of central 5-HT activation (flat body posture, forepaw extension, abducted hindlimbs and occa-

TABLE 1

DESCRIPTION OF DRUGS USED IN THE PRESENT STUDY

Drug	Salt	Demonstrated receptor agonist effect	References and comments
8-Methoxy-2-(di-n-propylamino)tetralin (8-OMe-DPAT)	hydrochloride	5-HT	[40]
(+)-8-Methoxy-2-(di-n-propylamino)tetralin	hydrochloride	5-HT	[8, 9, 40]
(−)-8-Methoxy-2-(di-n-propylamino)tetralin	hydrochloride	5-HT	[8, 9, 40]
8-Hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT)	hydrobromide	5-HT	[8, 9, 40]
5-Hydroxy-2-(di-n-propylamino)tetralin (5-OH-DPAT)	hydrobromide	DA	[19,28]
d-Lysergic acid diethylamide (LSD-25)	tartrate	5-HT, DA	[33] Hallucinogenic.
2,5-Dimethoxy-4-methylamphetamine (DOM)	hydrochloride	5-HT	[38] Hallucinogenic
Quipazine	hydrogen maleate	5-HT, DA, NA	[15, 17, 18, 20]

Except for LSD-25 (Sandoz Ltd., Basel), all drugs have been synthesized in our laboratories.

sionally tremor in the forepaws). The demonstration that the "5-HT syndrome" induced by one of these compounds, 8-OH-DPAT was not blocked by 5-HT depletion by means of reserpine plus the tryptophan hydroxylase inhibitor alpha-propyldopacetamide (H22/54) strongly supports the view of direct 5-HT receptor stimulating effect [9].

In view of the established role of central 5-HT in the mediation of male rat sexual behavior, we have tested the effects of two of these new compounds, i.e., 8-OMe-DPAT and 8-OH-DPAT (Fig.1), on this behavior. (The synthesis of 8-OMe-DPAT has been reported previously [6]. However, its pharmacology has not been described.) The aim of our testing was to further elucidate central monoaminergic mechanisms mediating sexual behavior in the male rat, and we have also included some reference drugs for comparison in the study.

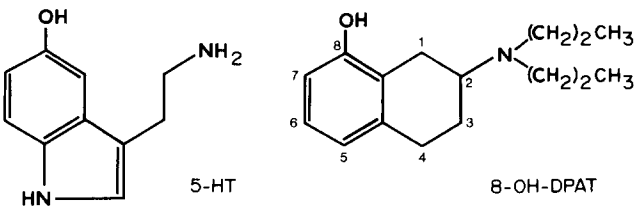

FIG. 1. Structure formula of 8-OH-2-(di-n-propylamino) tetralin (8-OH-DPAT). The structure formula of 5-hydroxytryptamine (5-HT) has been included for comparison.

METHOD

Animals

Male Wistar rats (Möllegaard, Vejle, Denmark), approximately 6 months of age at the start of the experiment, were used. They were housed, 4 per cage, under conditions of constant temperature and humidity with food and water available ad lib. The day-light cycle was artifically maintained (dark 11.00 a.m.–11.00 p.m.).

Drugs

The drugs used in this study are presented in Table 1. The drugs were dissolved in 0.9% saline and injected intraperitoneally in a volume of 2 ml/kg. Controls were given the saline vehicle.

Behavioral Testing Procedure

Mating tests were begun 2 hr after onset of darkness. The males were presented with a female brought into sexual receptivity by sequential treatment with estradiol benzoate (20 μg/animal), followed 42 hr later by progesterone (0.5 mg/animal) 6 hr before testing the animals. The mating tests were ended when one of the following conditions was fulfilled: (1) 15 min after the presentation of the female to the male, if at that time no mount with intromission had taken place; (2) 30 min after the first mount with intromission if no ejaculation had taken place; (3) 15 min after ejaculation if no mount with intromission had occurred subsequently; (4) after the first post-ejaculatory mount with intromission. The following behavior items were recorded: (1) Mount latency, i.e., time from the entrance of the female into the observation cage to the first mount without intromission; (2) Intromission latency, i.e., time from the entrance of the female into the observation cage to the first mount with intromission; (3) Mount frequency, i.e., number of mounts without intromission before ejaculation; (4) Intromission frequency, i.e., number of mounts with intromission before ejaculation; (5) Ejaculation latency, i.e., time from the first mount with intromission until ejaculation; (6) Post-ejaculatory interval, i.e., time from the ejaculation to the next mount with intromission.

Statistics

The following non-parametric procedures were used in the statistical evaluation of the results: Friedman two-way ANOVA followed by Wilcoxon matched-pairs signed-ranks test, Kruskal-Wallis one-way ANOVA followed by Mann-

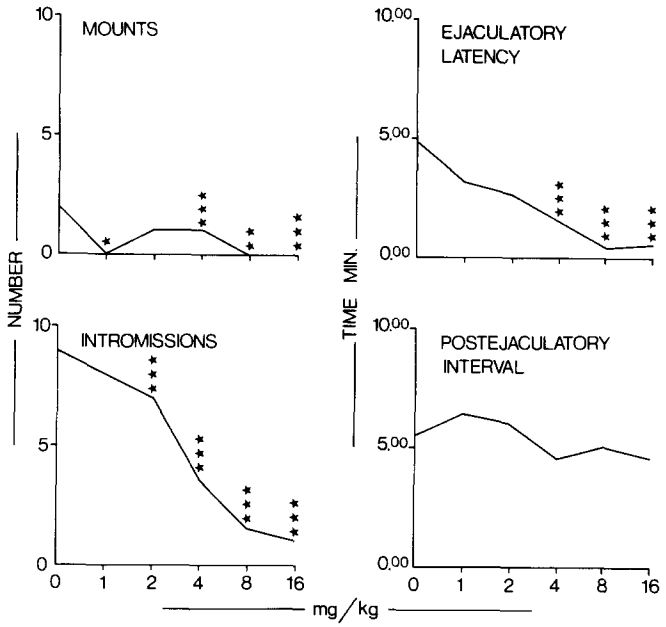

FIG. 2. Effects of 8-OMe-DPAT on male rat sexual behavior. The figure shows the results of two separate experiments: 0, 1 and 2 mg/kg (n=12) and 0, 4, 8 and 16 mg/kg (n=14). The drug or saline vehicle was given 15 min before presenting the male with a female. Using a balanced design the animals served as their own controls in the two experiments respectively. Shown are the medians and the two control groups are represented by the grand median. Statistical comparisons with the respective control group were made by means of Wilcoxon matched-pairs signed-ranks test. *$p<0.05$; **$p<0.02$; ***$p<0.01$.

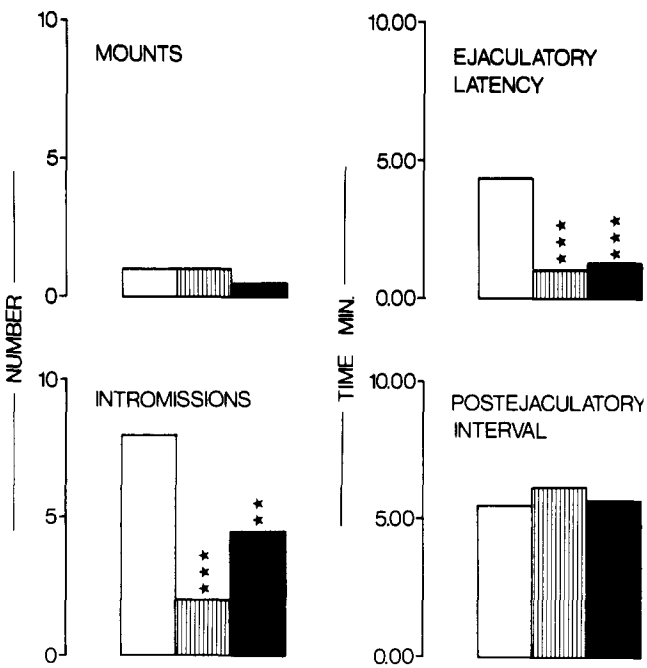

FIG. 3. Effects of (+)-8-OMe-DPAT and (−)-8-OMe-DPAT on male rat sexual behavior. The animals (n=20) were given the two isomers at a dose of 4 mg/kg IP 15 min before presenting the male with a female. Shown are the medians of the same animals given all treatments using a balanced design. Statistical evaluation was performed by means of Wilcoxon matched-pairs signed-ranks test. **$p<0.02$; ***$p<0.01$. □ Controls; ▥ (+)-8-OMe-DPAT; ■ (−)-8-OMe-DPAT.

Whitney U test [37] and a multivariate ANOVA [27]. Results are represented by medians in figures and tables. $p>0.05$ (two-tailed) was considered as non-significant.

RESULTS

Effects of 8-OMe-DPAT

The administration of 8-OMe-DPAT in doses up to 16 mg/kg IP (−15 min), produced a dose-dependent decrease in the number of mounts and intromissions, and a shortening of the ejaculatory latency (Fig.2). At the doses of 8 and 16 mg/kg, 3 animals in each group ejaculated already at the first intromission. No statistically significant changes were seen in the other behavioral items recorded. All animals, particularly at higher doses, displayed marked signs of hind limb abduction (cf.[21]).

Effects of (+)-8-OMe-DPAT and (−)-8-OMe-DPAT

There were no statistically significant differences between (+)-8-OMe-DPAT and (−)-8-OME-DPAT, 4 mg/kg IP (−15 min), in behavioral effects although the former enantiomer tended to have a stronger effect on the number of intromissions (Fig. 3). Both drugs produced a significant reduction in the number of intromissions and a significant shortening of the ejaculatory latency. No significant changes were observed in any of the other behavioral items recorded.

Effects of 8-OMe-DPAT in Castrated Male Rats

The animals had no preoperative sexual experience. When tested 4 weeks after castration, the animals showed no signs of sexual activity. The animals were thereafter given 8-OMe-DPAT in the doses 0, 2 or 8 mg/kg IP (−15 min) every second day for twelve days (Fig.4). There was a dose-dependent increase in the number of mounts and a smaller, though statistically not significant, increase in the number of intromissions. One of 9 animals treated with 8 mg/kg ejaculated. No ejaculations were observed when the animals were given 0 or 2 mg/kg. In a final test the drug treatment was discontinued and all signs of sexual behavior disappeared.

Except for one mount by one animal in the first post-operative test, there were no signs of sexual activity during control sessions.

Effects of 8-OH-DPAT

The administration of 8-OH-DPAT, in doses up to 4 mg/kg IP (−15 min) produced a significant and dose-dependent reduction in the number of intromissions preceding ejaculation and a significant shortening of the ejaculation latency (Fig.5). At the highest doses, 1, 2 and 4 mg/kg, 1, 3 and 3 animals, respectively, ejaculated already at the first intromission. In addition, 8-OH-DPAT in the dose interval 0.125–0.5 mg/kg produced a significant reduction in the

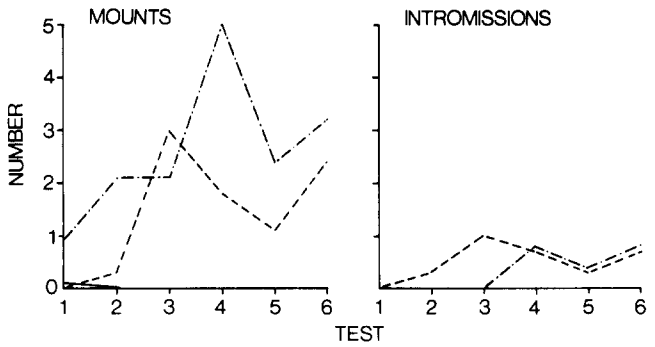

FIG. 4. Effects of 8-OMe-DPAT on the sexual behavior in castrated male rats. Three groups of animals were used: 0 mg/kg (n=9), 2 mg/kg (n=9) and 8 mg/kg (n=9). The animals were given the drug or saline vehicle IP 15 min before presenting the male with a female and tested every second day beginning four weeks after the castration. The median cumulative performance of the respective group is shown in the figure. The drug-treated groups were compared to the saline-treated controls by means of a non-parametric multivariate ANOVA. 2 mg/kg: Mounts $p<0.05$, Intromissions N.S. 8 mg/kg: Mounts $p<0.01$, Intromissions N.S. —— (0 mg/kg) --- (2 mg/kg) —·—·— (8 mg/kg).

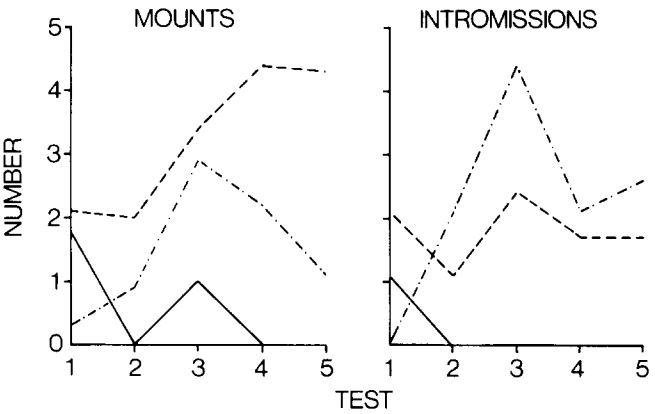

FIG. 6. Effects of 8-OH-DPAT on the sexual behavior in castrated male rats. Three groups of animals were used: 0 mg/kg (n=9), 0.25 mg/kg (n=9) and 0.5 mg/kg (n=9). The animals were given the drug or saline vehicle IP 15 min before presenting the male with a female. The tests were begun 4 weeks after castration and continued every second–third day for 9 days. The median cumulative performance of the respective group is shown in the figure. The respective treatment group was compared to the saline-treated controls by means of a non-parametric multivariate ANOVA. 0.25 mg/kg: Mounts $p<0.001$, Intromissions $p<0.01$. 0.5 mg/kg: Mounts $p<0.01$, Intromissions $p<0.01$. —— (0 mg/kg) -- (0.25 mg/kg) —·— (0.5 mg/kg).

post-ejaculatory latency. Doses below 0.125 were found to be without any statistically significant effects on the sexual behavior. The general appearance of these animals was similar to that observed after administration of 8-OMe-DPAT.

Effects of 8-OH-DPAT in Castrated Male Rats

As in the corresponding experiment using 8-OMe-DPAT, the animals had no preoperative experience, and there were no signs of sexual activity when tested 4 weeks after castration.

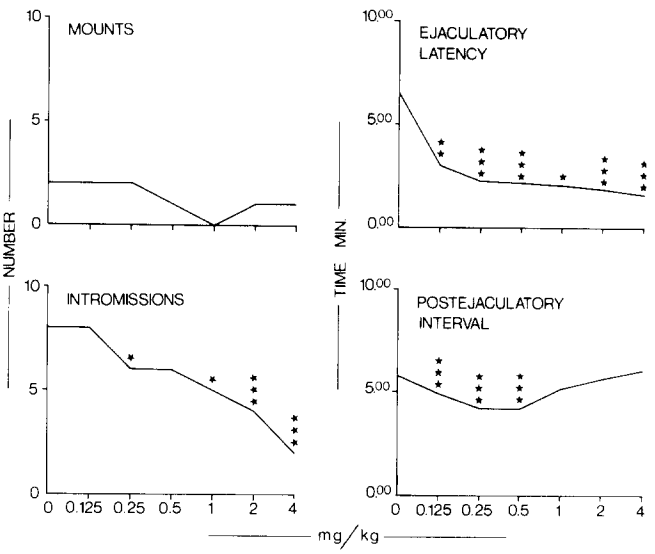

FIG. 5. Effects of 8-OH-DPAT on male rat sexual behavior. The animals were given 8-OH-DPAT, 0–4 mg/kg IP 15 min before presenting the male with a female. All animals (n=17) received each of the different treatments using a balanced design. The median values of the respective group are shown in the figure. Statistical comparison with the control group was made by means of Wilcoxon matched-pairs signed-ranks test. $*p<0.05$; $**p<0.02$; $***p<0.01$.

Thereafter three groups of animals were given 8-OH-DPAT in the doses 0, 0.25 or 0.5 mg/kg IP (−15 min) every second–third day for 9 days (Fig.6). There was a significant increase in the number of mounts and intromissions in the drug-treated groups. Two of the nine animals given 0.25 mg/kg and four of the nine animals given 0.5 mg/kg of 8-OH-DPAT ejaculated. In a final test the animals were tested without any drug treatment. One animal given 0.25 mg/kg displayed four mounts. No animals in any of the other groups displayed any signs of sexual activity.

Except for one mount and one intromission by a single animal in the first test and one mount by two animals in the third, there were no signs of sexual activity in the saline treated controls during the five test sessions.

Effects of 5-OH-DPAT

The administration of 5-OH-DPAT in doses up to 0.4 mg/kg IP (−15 min) produced a significant reduction in the number of mounts and intromissions and a significant shortening of the ejaculatory latency (Fig. 7). There were no effects on the post-ejaculatory interval. The effects obtained are not as marked as seen after 8-OMe-DPAT or 8-OH-DPAT and do not appear to be dose-dependent in the present dose interval. In a separate experiment higher doses (0.75–1.5 mg/kg) were found ineffective, whereas a further increase in dose (3.0–6.0 mg/kg) reduced the number of copulating animals without any major effects on any of the different behavioral items recorded. At these higher doses there were signs of increased sniffing and gnawing, but these effects were not noticed in the dose range presented in Fig. 7.

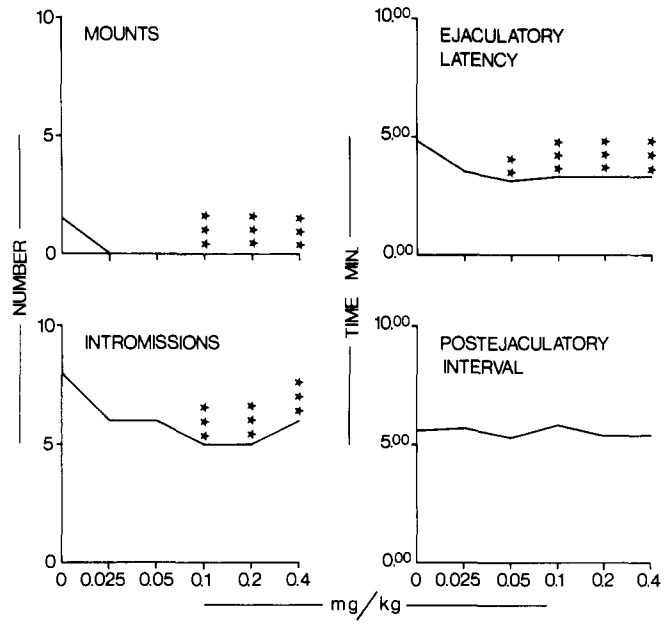

FIG. 7. Effects of 5-OH-DPAT on male rat sexual behavior. The figure shows the results from two separate experiments: 0, 0.025, 0.05 and 0.1 mg/kg (n=18) and 0, 0.1, 0.2 and 0.4 mg/kg (n=17). The drug or saline vehicle was given 15 min before presenting the male with a female. Using a balanced design the animals served as their own controls in the two experiments. Shown are the medians and the two duplicated treatments, 0 and 0.1 mg/kg, are represented by their grand medians in the figure. Statistical comparisons with the respective control group were made by means of Wilcoxon matched-pairs signed-ranks test. $^{**}p<0.02$, $^{***}p<0.01$.

TABLE 3

EFFECTS OF QUIPAZINE ON MALE RAT SEXUAL BEHAVIOR

	Quipazine (mg/kg)			
Behavioral item	0	0.375	0.75	1.5
Number of mounts	3	5	3	5.5
Number of intromissions	7.5	9.5	9	11.5
Ejaculation latency (min)	7.15	8.85	7.65	9.15
Postejaculation interval (min)	5.40	5.45	5.90	5.95
Number of ejaculating animals	14	14	14	12
Number of animals	14	14	14	14

The animals were given the drug 15 min before presenting the male with a female. Using a balanced design the animals served as their own controls.

Statistical evaluation by means of Friedman two-way ANOVA by ranks. No group differences were found.

Effects of LSD-25, Quipazine and DOM

None of these agents were found to have any stimulating effect on the sexual behavior. In addition to the data shown in Table 2, LSD-25 was given in a dose of 0.02 mg/kg without any statistically significant effect on the sexual behavior and in a dose of 1 mg/kg with the result that 6 out of 9 animals failed to initiate copulation. Quipazine given at high doses (3.0 and 6.0 mg/kg) produced a decrease in the number of ejaculating animals (Tables 2–4).

TABLE 2

EFFECTS OF *d*-LYSERGIC ACID DIETHYLAMIDE ON MALE RAT SEXUAL BEHAVIOR

	d-Lysergic acid diethylamide (mg/kg)			
Behavioral item	0	0.125	0.25	0.5
Number of mounts	1	4	1	5.5
Number of intromissions	9	7	6	7.5
Ejaculation latency (min)	2.75	3.75	2.25	5.20
Postejaculation interval (min)	5.55	6.25	6.40	6.10
Number of ejaculating animals	8	8	7	5
Number of animals	8	8	7	7

Four separate groups of animals were used. The drug was given 15 min before presenting the male with a female.

Statistical evaluation was performed by means of Kruskal-Wallis one-way ANOVA by ranks. No significant group differences were found.

TABLE 4

EFFECTS OF 2,5 DIMETHOXY-4-METHYL-AMPHETAMINE ON MALE RAT SEXUAL BEHAVIOR

	2,5 dimethoxy-4-methyl-amphetamine (mg/kg)			
Behavioral item	0	0.25	0.5	1.0
Number of mounts	2	2	4	12*
Number of intromissions	8	8	7	5
Ejaculation latency (min)	4.65	5.00	4.50	7.40
Postejaculation interval (min)	5.55	5.90	5.55	5.55
Number of ejaculating animals	18	18	17	11
Number of animals	18	18	18	18

The animals were given the drug 15 min before presenting the male with a female. The same animals were given all treatments using a balanced design.

Statistical evaluation by means of Friedman two-way ANOVA by ranks followed by Wilcoxon matched-pairs signed-ranks test. No group differences were found except for the mount frequency, $\chi^2=18.54$, $p<0.001$.

$^{*}p<0.01$.

DISCUSSION

The present experiments demonstrate an unique effect of 8-OMe-DPAT and 8-OH-DPAT on male rat sexual behavior.

The drugs caused a drastic decrease in the number of intromissions preceding ejaculation and a shortening of the ejaculatory latency, exceeding that so far reported after any other experimental treatment. Indeed, at some doses some of the animals ejaculated at the very first intromission. Relatively small alterations were seen in the post-ejaculatory interval even though a significant shortening was seen after some doses of 8-OH-DPAT.

Spontaneous ejaculations were never observed in conjunction with the drug treatment. Neither was male-to-male mounting, which may occur in the home cage following a drug treatment, nor merely mounting of the female observed to induce ejaculation. Normally ejaculation is achieved after several successive intromissions distributed over a 5–10 min period. The decrease in the number of intromissions before ejaculation seen with 8-OMe-DPAT and 8-OH-DPAT suggests that these drugs caused an increase sensory feedback from the penile intromissions.

Besides altering the mating pattern of the intact male, administration of 8-OMe-DPAT or 8-OH-DPAT initiated copulation in males rendered sexually inactive by castration. Following the drug treatment part of the animals began to mount the female and even displayed a full mating pattern. This suggests that the drugs do not only influence the consummative phase of the sexual behavior but also its appetitive phase, with an increase in sexual motivation.

8-OH-DPAT seems to be roughly ten times as potent as 8-OMe-DPAT in eliciting stimulation of the male rat sexual behavior, which is quite similar to the relative biochemical potencies of the two drugs [40]. No significant difference in activity could be seen between (+)-8-OMe-DPAT and (−)-8-OMe-DPAT, although a somewhat more pronounced decrease in the number of intromissions was obtained for the (+) enantiomer. In biochemical and behavioral experimemts on the enantiomers of 8-OH-DPAT, the (+) enantiomer has been shown to be significantly more active than the (−) enantiomer though both enantiomers proved highly active [9].

Effects somewhat similar to those obtained with 8-OMe-DPAT and 8-OH-DPAT have been demonstrated following treatment with PCPA and the ergot derivative lisuride [2, 4, 36]. Both these drugs shorten the ejaculatory latency and may induce full sexual activity in castrated males without concomitant androgen treatment. A further indication that 5-HT may be involved in the effect of the sexual behavior is the observation that a disruption of the ascending 5-HT pathways by a localized injection of the neurotoxin 5,7-dihydrotryptamine (see [11]) into the dorsal medial mesencephalic tegmentum facilitates sexual behavior in castrated rats treated with subthreshold doses of testosterone [25]. Taken together, these and other findings [3,4] suggest an inhibitory role of central 5-HT on the expression of male rat sexual behavior (cf. [29]).

There is evidence that 8-OH-DPAT inhibits firing in 5-HT neurons of the dorsal raphe (T. H. Svensson, personal communication). Lisuride, besides activating central 5-HT receptors [22,23], is also known to inhibit firing in dorsal raphe 5-HT neurons [35]. Thus one possible explanation might be that activation of 5-HT autoreceptors is the predominant effect of this drug as well as of lisuride on the serotonergic system involved in the mediation of sexual behavior of the male rat. However, in an additional experiment, we found that the administration of 5-HTP, 25 mg/kg IP (−60 min) in combination with benserazide, 25 mg/kg IP (−90 min) did not antagonize the efects of 8-OH-DPAT, 0.25 mg/kg IP (−15 min). Treatment with 5-HTP produced an increase in the ejaculation latency to 225% of controls ($p<0.02$, Wilcoxon T-test), whereas the result after 8-OH-DPAT, alone and in combination with 5-HTP, was a decreased ejaculation latency to 30% ($p<0.001$) and to 60% ($p<0.05$) of controls, respectively. An alternative explanation would be that 8-OMe-DPAT and 8-OH-DPAT act as antagonists on postsynaptic 5-HT receptors involved in sexual behavior.

The concept that male-to-male and female-to-female mounting induced in the rat by lisuride is mediated via a simultaneous activation of central postsynaptic DA receptors and 5-HT autoreceptors [14] might be relevant also for the heterosexual behavior. However, the high 5-HT receptor specificity for 8-OH-DPAT and 8-OMe-DPAT as observed biochemically indicate that the DA component is not essential. Experiments combining these drugs with DA receptor agonists and antagonists may throw further light on this question. We have combined PCPA, 100 mg/kg × 4 IP in daily doses (−24 hr) with 5-OH-DPAT, 0.1 mg/kg IP (−15 min) and found a stronger effect on the ejaculation latency than the effects produced by either drug alone. The effect on the ejaculation latency by PCPA and 5-OH-DPAT was a decrease to 67% ($p>0.05$, Wilcoxon T-test) and 49% ($p<0.02$) of controls, respectively. When combined the two drugs caused a decrease in the ejaculation latency to 29% of controls ($p<0.02$, in comparison with all other treatments). However, the strong effects induced by 8-OMe-DPAT or 8-OH-DPAT could not be reproduced.

Central serotonergic receptor stimulation by drugs has been widely coupled to hallucinogenic properties. However, LSD-25 and DOM, both drugs known as direct 5-HT receptor agonists with strong hallucinogenic effects in man, were ineffective in stimulating the male rat sexual behavior. Thus, there does not seem to be any correlation between hallucinogenic properties in man and stimulation of male rat sexual behavior. This is also supported by the activity on sexual behavior of the nonhallucinogenic ergot derivative lisuride [5]. Quipazine, by some groups considered to be a direct 5-HT receptor agonist ([18], cf. [20]) was also included in the present experiments. However, no stimulation of the sexual behavior was observed.

The morphine antagonists naloxone and naltrexone produce a shortening of the ejaculatory latency according to recent reports [32, 33, 34]. The possibility of an interaction between encephalin and 5-HT neurons on sexual behavior warrants further exploration.

In conclusion, the new type of 5-HT receptor agonists 8-OMe-DPAT and 8-OH-DPAT have been found to produce a highly dramatic reduction in the ejaculation latency and in the number of intromissions to ejaculation in the male rat. Current pharmacological means of activating central 5-HT receptors produce the opposite effect. In fact, a reduction in central 5-HT receptor activation is associated with effects in the same direction as those produced by 8-OMe-DPAT and 8-OH-DPAT. Present knowledge of the biochemical actions of these new drugs does not allow a precise conclusion on their mechanism of action. On the assumption that these aminotetralines act at central 5-HT receptors we suggest that the drugs act preferentially as agonists at 5-HT autoreceptors or, alternatively as 5-HT receptor antagonists in certain brain areas, including those parts mediating male rat sexual behavior.

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