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Differential Effects of a New Serotoninomimetic Drug, 8-OH-DPAT, on Copulatory Behavior and Pelvic Thrusting Pattern in the Male Rat

G. MORALI AND K. LARSSON

División de Neurociencias, Unidad de Investigación Biomédica
Instituto Mexicano del Seguro Social, Apartado Postal 73-032, México 03020, D.F.

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MORALI, G. AND K. LARSSON. *Differential effects of a new serotoninomimetic drug, 8-OH-DPAT on copulatory behavior and pelvic thrusting pattern in the male rat.* PHARMACOL BIOCHEM BEHAV **20**(2) 185–187, 1984.— Treatment of sexually experienced male rats with 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), a new drug having central serotoninomimetic activity, caused a dose-dependent decrease in the number of mounts and intromissions to ejaculation and shortened the ejaculation latency. These changes in the coital pattern were not accompanied by any marked changes in the organization of the thrusting pattern. It was concluded that treatment with 8-OH-DPAT may influence the excitability of the central neural circuits determining the elicitation of ejaculation without affecting those involved in the pelvic thrusting pattern, despite evidence of general motor disturbances.

Rat copulatory pattern Pelvic thrusting Serotoninomimetic drugs 8-OH-DPAT

WE recently reported that treatment of male rats with 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), a new drug that elicits pronounced biochemical and behavioral alterations indicative of central serotoninomimetic activity, exerts a remarkable stimulatory effect upon the masculine sexual behavior of male rats [1]. The rats were found to ejaculate after fewer intromissions and with a shorter latency than normal. However, the drug treatment also caused deviations in normal locomotor behavior and in body posture adjustment, indicating general motor disturbances. We therefore, decided to investigate whether treatment with 8-OH-DPAT induces changes in the motor components of the sexual behavior, especially the pelvic thrusting pattern, accompanying mounting [2,3].

METHOD

Animals were 12 adult sexually experienced male Wistar rats bred in our laboratory. They were maintained in single cages, fed with Purina and water ad lib in a room at 23°C under a reversed light-dark cycle (14 hr light). For sexual behavior testing, the male was placed in a cylindrical observation cage and, after a 5 min adaptation period, presented with a stimulus female which was brought into estrus by sequential treatment with estradiol benzoate (20 μg/animal) followed 42 hr later by progesterone (0.5 mg/animal) 6 hours before testing.

Mating tests were begun 2 hr after the onset of darkness. 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.

The technique for recording the copulatory movements has been described in detail elsewhere [3]. A cloth harness was designed to fit tightly to the rat without causing discomfort. The harness carried a strain gauge transducer (Grass SPA 01, 12 g weight) that measures acceleration in one plane. The accelerometer was connected to a DC Grass preamplifier coupled to a GRASS S8 polygraph. The amplitude (millivots), duration, and frequency of the signals generated during copulation were measured and analyzed as has been described previously [3].

Using a balanced design, the animals were treated with 0, 0.25, and 2 mg/kg of 8-OH-DPAT. The drug was dissolved in 0.9% saline and injected in a volume of 0.1 ml, 15 min before

TABLE 1

EFFECTS OF TREATMENT WITH 8-OH-DPAT UPON VARIOUS PARAMETERS OF SEXUAL ACTIVITY OF INTACT RATS

Behavior Parameter	Saline	8-OH-DPAT 0.25 mg/kg	8-OH-DPAT 2 mg/kg
No. of mounts	8.1 ± 8.3 (11)	2.5 ± 2.7* (6)	1.0† (1)
No. of intromissions	5.3 ± 1.8 (11)	3.2 ± 2.4‡ (11)	1.9 ± 1.1§ (8)
Mount Latency (sec)	11.5 ± 10.6 (11)	98.0 ± 189.4 (11)	165.0 ± 240.5 (9)
Intromission Latency (sec)	86.4 ± 149.2 (11)	137.9 ± 192.9 (11)	165.0 ± 240.5 (9)
Ejaculation Latency (sec)	391.4 ± 218.3 (11)	217.3 ± 235.2 (11)	147.2 ± 154.8* (9)
Post Ejaculatory Intervals (sec)	434.1 ± 204.0 (11)	393.3 ± 194.9 (11)	266.4 ± 120.4 (9)

Data represent mean of individual scores ± SD. Number of responsive Ss for each parameter is given in parentheses. Group comparisons were based upon the Student t-test (two-tailed).

*$p<0.05$; †$p<0.02$; ‡$p<0.01$; §$p<0.001$ Compared to saline-treated group.

presenting the male with a female. Each male was tested once with each dose, at 10-day intervals.

RESULTS AND DISCUSSION

Following the drug treatment, the animals appeared slightly sedated, particularly at the higher dose level. Animals treated with 2 mg/kg of 8-OH-DPAT showed a conspicuous behavioral syndrome consisting of a flat body posture, forepaw extension, and abducted hind limbs. All animals ejaculated after receiving 0.25 mg/kg of 8-OH-DPAT while 3 males failed to initiate any sexual activity after the administration of 2 mg/kg of the drug. The administration of 8-OH-DPAT produced a dose-dependent decrease in the number of mounts and intromissions before ejaculation, and a shortening of the ejaculation latency (Table 1). At the higher dose level, mounts were almost abolished (only one mount was shown by one male), and one male ejaculated at the very first intromission; indeed, when starting to copulate after the end of the postejaculatory period, the male again ejaculated without preceding intromission. No statistically significant deviations were seen in other behavioral components.

Following treatment with 0.25 mg/kg of 8-OH-DPAT, a statistically significant prolongation was found in the duration of the thrusting train at mounting. No corresponding changes were seen in the thrusting train accompanying intromission. At ejaculation, two patterns of thrusting train are usually recognized, one consisting of three thrusting phases of different amplitudes and another, of shorter duration, consisting of only one thrusting phase (Fig. 1 and Table 2). The saline-treated rats showed an equal proportion of long and short ejaculation patterns while animals treated with 2 mg/kg of 8-OH-DPAT tended to show a higher proportion of long ejaculation patterns. This tendency was, however, not confirmed statistically ($\chi^2=1.174$ NS). A general appreciation of the polygraphic records revealed that there are no major differences in the vigour of thrusting among the experimental conditions.

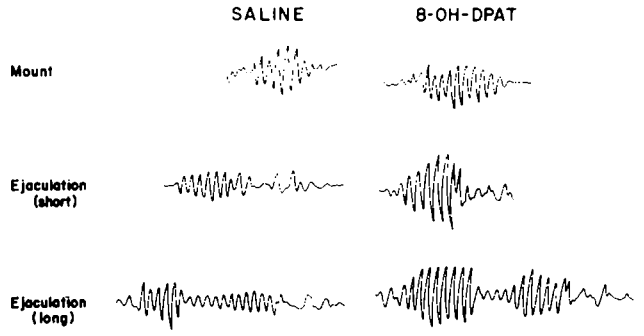

FIG. 1. Accelerometer records of mounts, and of the two types of ejaculatory patterns shown by male rats treated with either saline or 8-OH-DPAT. Note the similar organization of the pelvic thrusting in both groups. No differences were found between 0.25 and 2 mg/kg of 8-OH-DPAT. Thus, no indication is given here of the dose level used.

It may be assumed that the neural substrate for sexual behavior includes both circuits mediating the occurrence of ejaculation, and circuits that determine the pelvic thrusting pattern. According to the present findings, treatment with 8-OH-DPAT lowered drastically the threshold for the elicitation of the ejaculation response but had only minor effects upon the motor copulatory pattern. The failure of the drug to influence the motor copulatory pattern is particularly notable in view of the deficits caused by the drug treatment in the animal's ability to move and to adjust its body posture.

Present knowledge of the biochemical action of 8-OH-DPAT does not allow a precise conclusion on its mech-

TABLE 2

CHARACTERISTICS OF THE MOTOR COPULATORY PATTERN OF MALE RATS TREATED WITH EITHER SALINE OR 8-OH-DPAT

Behavior Parameter	Saline	8-OH-DPAT 0.25 mg/kg	8-OH-DPAT 2 mg/kg
Mean Duration (sec)			
Mount	0.467 ± 0.10	0.641 ± 0.17*	—
Intromission	0.350 ± 0.10	0.363 ± 0.08	0.444 ± 0.15
Ejaculation	0.622 ± 0.15 (5)	0.576 ± 0.11 (5)	0.799 ± 0.15 (2)
	1.102 ± 0.19 (6)	1.236 ± 0.10 (7)	1.194 ± 0.19 (7)
Mean frequency per sec of pelvic movements			
Mount	17.63 ± 0.51	17.93 ± 1.16	—
Intromission	18.83 ± 1.09	18.22 ± 0.66	18.53 ± 1.04
Ejaculation	18.74 ± 0.60	17.82 ± 1.24	18.92 ± 1.34

Data represent mean of individual means ± SD. Numbers in parentheses correspond to number of subjects.

*$p<0.02$ Compared to saline group.

anism of action [1,4]. Biochemical data indicate that this compound is a potent postsynaptic 5-HT receptor agonist [4] lacking appreciable effects on central catecholamine receptors.

Further evidence for the serotonergic activity of 8-OH-DPAT is found in the fact that, like the 5-HT precursor 5-HTP, it produces a behavioral syndrome, including flat body posture, forepaw extension and abducted hind limbs, which has been attributed to stimulation of post-synaptic serotonergic receptors [5,6].

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