ELSEVIER

European Journal of Pharmacology 309 (1996) 21–24

ejp

Short communication

Dopamine receptor antagonists attenuate conditioned place preference following sexual behavior in female Syrian hamsters

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Received 17 May 1996; accepted 21 May 1996

Abstract

We assessed the effects of the dopamine D_2 receptor antagonists, sulpiride and raclopride, on conditioned place preference produced by sexual behavior in female Syrian hamsters. Female hamsters treated with sulpiride or raclopride showed high levels of sexual behavior (lordosis) that were equivalent to control females receiving vehicle injections. The degree of place preference conditioning for sulpiride-treated females was marginally reduced, whereas females treated with raclopride showed no evidence of conditioning. These results indicate that conditioned place preference is a useful means for probing the appetitive components of female sexual behavior, and that dopamine D_2 receptors are involved in this appetitive process.

Keywords: Conditioned place preference; Sulpiride; Raclopride; Dopamine; Dopamine D_2 receptor; Lordosis

1. Introduction

Conditioned place preference procedures have been used effectively to investigate appetitive processes (Hoffman, 1989). In the conditioned place preference paradigm, the repeated association of a rewarding stimulus or event with one compartment of a multicompartment chamber will increase the amount of time the animal spends in that compartment in the absence of the reward (Bozarth, 1987). We have demonstrated that female Syrian hamsters acquire a conditioned place preference following sexual or aggressive interactions with a male hamster (Meisel and Joppa, 1994). Dopamine receptor antagonists have been shown to be particularly effective in disrupting many appetitive processes, including the acquisition of a conditioned place preference (Blackburn et al., 1992; Salamone, 1994). Because dopamine D_2 receptor antagonists do not disrupt, and may even enhance, the expression of female sexual behavior (Foreman and Hall, 1987; Grierson et al., 1988), we reasoned that administration of dopamine D_2 receptor antagonists should be able to block the appetitive components of sexual behavior without any effect on the expression of the behavior itself. In this study, female Syrian hamsters received either sulpiride or raclopride in conjunction with conditioned place preference induced by sexual behavior in an attempt to dissociate pharmacologically the appetitive and consummatory components of female sexual behavior.

2. Materials and methods

2.1. Subjects

Subjects were 51 adult female Syrian hamsters (received from either Sasco or Charles River Breeding Laboratories) about 60 days old at arrival. Adult male Syrian hamsters served as stimulus animals for the lordosis behavior tests. Females were housed singly and males were housed in groups of 3–4 in clear plastic cages (50.8 × 40.6 × 20.3 cm), in a colony room maintained at 22°C on a 14 : 10 light cycle with lights out at 13.30 h. Food and tap water were available throughout the experiment.

2.2. Apparatus

The conditioned place preference apparatus was described previously (Meisel and Joppa, 1994). Briefly, two compartments (60 × 45 × 38 cm), one white and one gray,

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PII S0014-2999(96)00389-5

were connected by a clear central compartment (37 × 22 × 38 cm). Sliding partitions of the same color as the compartments were used to isolate the females during conditioning. To further distinguish the compartments, the gray chamber had Aspen pine bedding (the same bedding as in the females' home cages) and the white compartment contained bed-o'-cobs (1/8″) bedding.

2.3. Conditioning and testing procedures

Females were bilaterally ovariectomized while anesthetized with pentobarbital (7.5 mg/100 g body weight) within 2 days of arrival. Three to 4 weeks later females were injected s.c. with 10 μg of estradiol (in 0.1 ml cottonseed oil) followed 2 days later by an s.c. injection of 500 μg of progesterone (in 0.1 ml cottonseed oil). This regimen is sufficient to induce lordosis in females if paired with a male. Four to 6 h after receiving progesterone, the females were given a preference pre-test, which consisted of placing each female in the central chamber of the apparatus and allowing her to roam freely between the gray and white compartments for 10 min. The amount of time spent individually in the gray and white compartments was recorded. All behavioral testing was conducted under ambient fluorescent illumination within 3 h of the onset of the dark portion of the daily cycle in the colony room.

During the conditioning sessions, the hormone regimen given prior to the preference pre-test was repeated weekly for 5 weeks. Fifteen of the hamsters were injected i.p. with sulpiride (12 mg/kg body weight in 45% cyclodextrin) 1.5–2 h before conditioning (sulpiride and cyclodextrin were obtained from Research Biochemicals International, USA). Because some drug remained suspended in the cyclodextrin solution the dose of sulpiride is approximate. An additional 24 females were injected i.p. 15 min before the start of conditioning with either 0.25 or 1.25 mg/kg of raclopride (Research Biochemicals International) dissolved in deionized water. The difference in the timing of the sulpiride and raclopride injections reflects the poor absorption of sulpiride into the brain following systemic injection (Nishibe et al., 1982). Twelve other females received a control injection of the cyclodextrin vehicle at the same time the sulpiride injections were given. Conditioning sessions were conducted at least 4 h after the progesterone injection. For conditioning, females receiving sulpiride ($n = 8$), 0.25 mg/kg raclopride ($n = 8$), 1.25 mg/kg raclopride ($n = 8$), or control vehicle injections ($n = 7$) were paired with a male hamster in the gray compartment for 10 min, and then placed alone in the white compartment about 1 h later. During the 10 min session with the male, the total amount of time the females remained in the lordosis posture (defined by a dorsoflexion of the female's back such that the back was either flat or concave) was recorded. Additional control groups of females receiving either sulpiride ($n = 7$), raclopride ($n = 8$ combined for both doses), or the cyclodextrin vehicle ($n = 5$) were placed alone in both the gray and white compartments.

One week after the last conditioning session, females were again treated with estradiol and progesterone and given a post-conditioning preference test 4–5 h after progesterone injection. As in the pre-test, females were placed in the center, clear compartment and allowed free access to the gray and white compartments for 10 min. Again, the amount of time spent individually in the gray and white compartments was recorded.

3. Results

All groups of female hamsters displayed high levels of lordosis during the conditioning sessions with the male regardless of drug or vehicle treatment (Fig. 1). There were no significant effects of sulpiride or raclopride treatments on the expression of lordosis over the course of the individual conditioning sessions, nor were there any obvious effects of these drugs on the general behavior of these animals.

Fig. 2 compares the amount of time spent in the gray compartment during the pre- and post-tests by female hamsters in each group. Vehicle-treated females paired with a male (and engaging in sexual behavior) spent a significantly greater portion of the post-test compared with the pre-test in the gray compartment, $t(6) = 3.29$, $P < 0.02$. For sulpiride-treated females paired with a male there was a nonsignificant trend for an increase in the amount of time spent in the gray compartment on the post-test, $t(7) = 2.18$, $P < 0.07$. In contrast, neither group of raclopride-treated females showed any evidence of a change in the time spent in the gray compartment. There was no evidence of a significant difference between pre- and post-tests in the time spent in the gray compartment for either the vehicle or sulpiride-treated control females not paired with a male, though there was a significant decrease in the amount of time spent in the gray compartment for

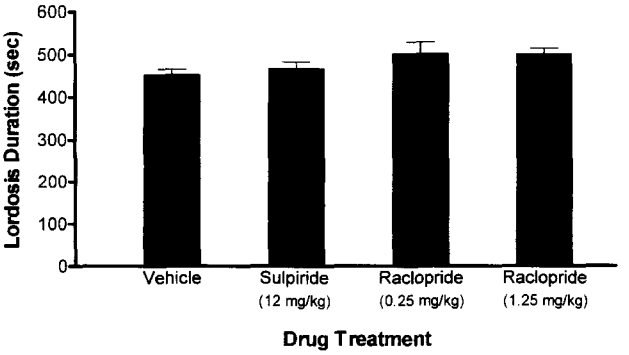

Fig. 1. Mean (±S.E.M.) lordosis durations (averaged across the five tests) for the females during the conditioning sessions with the male. Females in all groups showed high levels of lordosis, and there were no significant group differences.

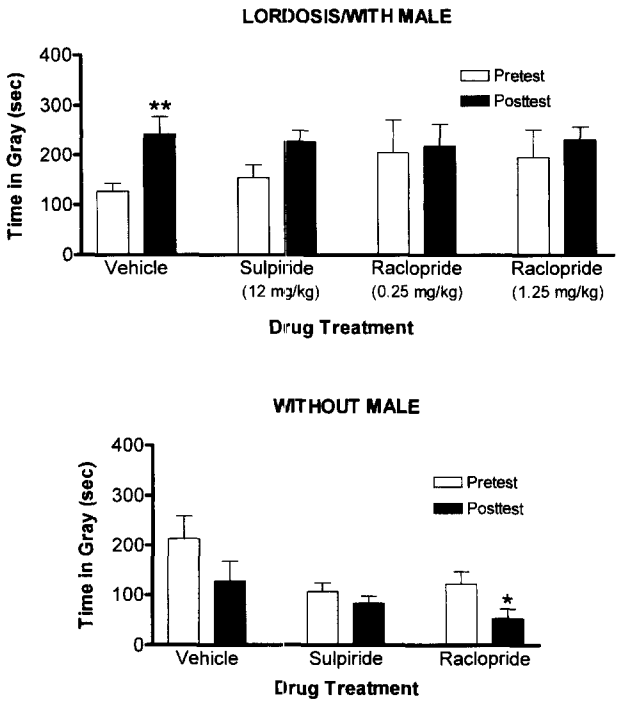

Fig. 2. Mean (±S.E.M.) number of seconds during the pre-conditioning (Pre) and post-conditioning (Post) preference tests that the hamsters in each treatment group spent in the gray compartment. The lordosis groups (top) were paired with a male and engaged in sexual behavior in the gray compartment, whereas the control groups (bottom) were not paired with a male in either compartment. * $P < 0.03$ vs. pre-conditioning test; ** $P < 0.02$ vs. pre-conditioning test.

the raclopride-treated control females, $t(8) = 2.73$, $P < 0.03$.

4. Discussion

The results of this study replicate our previous finding of a conditioned place preference following sexual behavior in female hamsters (Meisel and Joppa, 1994). These studies indicate that conditioned place preference is an effective procedure to study the appetitive components of female sexual behavior.

Studies of conditioned place preference using various rewarding stimuli consistently implicate dopaminergic pathways in support of this type of conditioning (Hoffman, 1989). Raclopride, in our study, completely prevented the acquisition of a conditioned place preference induced by female sexual behavior. In contrast, another dopamine D_2 receptor antagonist, sulpiride, attenuated, but did not eliminate, this conditioned place preference. Because we examined the effectiveness of only one dose of sulpiride, it is possible that higher doses may have more completely antagonized dopamine D_2 receptors. Our results implicating dopamine D_2 receptors in the development of conditioned place preference do not contradict other observations that suggest roles for dopamine D_1 and D_3 receptors in the mediation of reward processes (Hoffman, 1989; Mallet and Beninger, 1994).

Some dopamine receptor agonists or antagonists have been shown to produce, respectively, conditioned place preference or conditioned place aversion in their own right (Hoffman and Beninger, 1989; Schechter and Meehan, 1994; White et al., 1991). Indeed, we found that raclopride significantly reduced the preference for the gray compartment in females not paired with a male. When sulpiride was given alone in our study it did not alter the females' preferences for the gray compartment, though this may be related to a lack of close temporal coupling between the administration of sulpiride and the onset of testing (1.5–2 h) rather than any ineffectiveness of dopamine receptor antagonism in this regard.

Our observations that neither dopamine D_2 receptor antagonist, sulpiride nor raclopride, disrupted the ability of female hamsters to display lordosis is consistent with previous studies suggesting that activation of dopamine D_2 receptors may actually inhibit the expression of female sexual behavior (Foreman and Hall, 1987; Grierson et al., 1988). In contrast, dopamine D_1 receptor activation may be important for the expression of lordosis, though the mechanism for this effect is uncertain (Mani et al., 1994). The fact that dopamine D_2 receptor antagonists, unlike dopamine D_1 receptor antagonists, can alter appetitive processes independently of any effect on the expression of sexual behavior will make compounds like sulpiride and raclopride invaluable for future studies of the motivational control of sexual behavior in females.

Acknowledgements

We would like to thank Andrew Greendorfer, Adam Hartman, Jason Ribisi, and Brian Schultz for their help with the behavioral testing and conditioning. This research was supported by NSF Grant IBN-9412543 and a grant from the Purdue Research Foundation.

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