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Fluoxetine does not prevent interspecific mating between two hamster species

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Abstract

In a recent study we showed that female Syrian hamsters (*Mesocricetus auratus*) from a laboratory stock readily mated with male Turkish hamsters (*M. brandti*). We hypothesized that captivity and/or unconscious selection of the most receptive females by researchers or animal caretakers results in heightened female sexual receptivity and reduces the tendency to reject heterospecific males. To test this hypothesis, we decided to decrease female receptivity by injection of fluoxetine, which increases the levels of serotonin in a number of brain loci, including areas involved in mediating sexual behavior, and determine whether such a decrease in receptivity would result in better discrimination of heterospecific males and rejection of such males as mates. We treated estrous female Syrian hamsters with 20 mg / kg fluoxetine or vehicle and paired them with both a conspecific and a heterospecific male (Turkish hamster) in two sequential tests. All females showed similar behavior – they exhibited lordosis toward both conspecific and heterospecific males. We did not observe any sign of aggression. Latency to display lordosis and the duration of lordosis were not affected by fluoxetine. Fluoxetine thus did not have an effect on the behavior of females toward conspecific or heterospecific males. Independent of treatment (fluoxetine or vehicle injection), females did display lordosis significantly faster and for a longer duration in the presence of a conspecific male, even though these differences were small.

Keywords

hamsters; *Mesocricetus*; serotonin; fluoxetine; lordosis; species discrimination

INTRODUCTION

It is normally assumed that estrous females are not sexually receptive toward males of closely related species, thus preventing costly inter-specific matings. In Turkish hamsters (*Mesocricetus brandti*), for example, estrous females descended from recently captured animals exhibited lordosis toward conspecific males but were aggressive and did not exhibit lordosis toward heterospecific (Syrian hamster, *M. auratus*) males [1]. In contrast, we have recently shown that such differential behavior toward conspecific and heterospecific males may have been lost in females after many generations in captivity [2]. Using Turkish hamsters

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descended from the same stock used by Murphy (1978), we replicated Murphy's experiment and found that females behaved similarly toward conspecific and heterospecific, Syrian hamster males. Specifically, estrous female Turkish hamsters were receptive toward heterospecific males and did not attack these males [2]. We found the same results when we tested female Syrian hamsters from our laboratory stock – they were receptive toward both conspecific and heterospecific (Turkish hamster) males [2]. We hypothesized that the decrease in discrimination against heterospecific males may be due to heightened sexual receptivity in these captive stocks, perhaps due to unconscious selection for sexually productive and non-aggressive females [2,3].

In order to test the hypothesis that long periods in captivity heightens sexual receptivity leading to interspecific mating we decided to experimentally reduce female sexual receptivity by treatment with a drug that alters neural function and female sexual receptivity. The hypothesis would be supported if drug treatment reduced receptivity in estrous females and blocked mating with heterospecific males. This approach could potentially provide a means to investigate the neural and/or hormonal mechanisms underlying species discrimination and differential reactions toward conspecific and heterospecific individuals. Especially interesting targets are hormones and/or neurotransmitters with major roles in aggression and/or sexual receptivity, such as serotonin and vasopressin [4–6].

The specific goal of this study was to investigate the role of serotonin in female sexual receptivity and aggression in female Syrian hamsters and, more specifically, to determine whether increased serotonin levels prevent females from mating with heterospecific males. To increase the neural levels of serotonin we used fluoxetine, a serotonin re-uptake inhibitor, which increases the levels of available serotonin in specific serotonergic brain regions [7]. It has been shown that fluoxetine can have an inhibitory effect on lordosis. For example, intact female rats injected daily for 2–3 weeks with 10 mg fluoxetine / kg showed a reduction in proceptive behavior (hop/darting and ear wiggling) [8], and less lordosis behavior than in control females [8,9]. Lordosis was also reduced in female rats with a single 20 mg / kg dose of fluoxetine [7]. Another serotonin agonist (8-OH-DPAT), injected into the medial preoptic area of female rats also reduced lordosis behavior and made females more resistant to males' mounting attempts [10]. Female Syrian hamsters given a single dose of fluoxetine during estrus showed decreased lateral displacement, the movement that female hamsters make with their perineum in response to male-like tactile stimulation [11,12]. These studies all suggest that systemic injections of fluoxetine may reduce the occurrence of lordosis in female hamsters. Such a decrease in female receptivity might also result in lower levels or even no receptivity toward heterospecific males by female Syrian hamsters.

METHODS

All animals were born and raised in captivity at Cornell University, Ithaca, NY. All research was conducted with approval from Cornell University's Institutional Animal Care and Use Committee (protocol #1993-0120). Hamsters were weaned at 30 days of age and housed singly in solid bottom polycarbonate cages (45×24×14.5 cm) with sani-chip bedding material and constant access to food (Prolab 1000, Agway, Syracuse, NY) and water. Syrian hamsters (*Mesocricetus auratus*) were maintained on a 14L:10D light-dark schedule with lights off between 10:00 and 20:00 hours (Eastern Standard Time). Male Turkish hamsters (*M. brandti*) were maintained on a 16L:8D light-dark schedule with lights off between 10:00 and 18:00 hours (Eastern Standard Time). Syrian and Turkish hamsters were maintained in separate rooms. Experiments were run within the first three hours of the dark phase (i.e., 10:00–13:00 hours). We used dim, indirect light to allow videotaping and observations.

We used 20 female Syrian hamsters, 20 male Syrian hamsters (conspecific males) and 20 male Turkish hamsters (heterospecific males). Females were 195 ± 54 (mean $\pm$ SD) days old and weighed 165 ± 23 g. Females were sexually naïve and had not interacted with any Turkish hamsters prior to this experiment. Females received an intraperitoneal injection of fluoxetine hydrochloride (Sigma Chemical; 20 mg / kg; dissolved in 20% dimethyl sulfoxide in 0.9% saline [vol / vol]) or vehicle. The volume injected depended on female body weight (approximately 0.2 ml). Tests occurred 80 min after the injection; we used this timing based on previous studies on the effect of fluoxetine in Syrian hamsters [12,13]. Females were tested twice, once with a conspecific male and once with a heterospecific male. At the beginning of each test session for a given female, a conspecific or a heterospecific male was introduced into the female's cage. We video-recorded their behavior for 5 min and later measured the number and duration of female attacks, latency to display lordosis and total duration of lordosis. After the first test, the male was returned to his cage. Ten minutes later the female was tested again, with a conspecific male if she had been tested with a heterospecific male in the first test, or vice versa. The order of the two tests was counterbalanced – there were no order effects ($P > 0.05$).

We used two, separate, repeated-measures GLM (General Linear Model) analyses to investigate the latency to display lordosis and lordosis duration. The within-subjects variable was species of the male (conspecific or heterospecific). The between-subjects variable was treatment (vehicle or fluoxetine). Neither the age nor the weight of the female affected any of the variables ($P > 0.05$). Normality was tested using the Kolmogorov-Smirnov test (all variables had a normal distribution, $P > 0.05$). Statistical analyses were carried out using SPSS 14.0 for Windows. Values shown represent mean $\pm$ SD.

RESULTS

All 20 estrous females displayed lordosis toward both the conspecific and heterospecific males. We did not observe any sign of aggression. Fluoxetine thus did not have an effect on the sexual behavior of females that we measured or on their responses toward conspecific versus heterospecific males. In all tests, females investigated the male before displaying lordosis. Latency to display lordosis was not affected by fluoxetine ($F_{1,18} = 0.36$, $P = 0.56$; Fig. 1), but females did display lordosis significantly faster in the presence of a conspecific male than in the presence of a heterospecific male, regardless of the drug treatment ($F_{1,18} = 13.79$, $P = 0.002$; Fig. 1). Similarly, the duration of lordosis was not affected by fluoxetine ($F_{1,18} = 0.49$, $P = 0.49$; Fig. 2), but females did spend more time in lordosis in the presence of a conspecific male than in the presence of a heterospecific male, regardless of the drug treatment ($F_{1,18} = 26.31$, $P < 0.0005$; Fig. 2).

DISCUSSION

Our results support a recent study showing that female Syrian hamsters in captivity will mate with male Turkish hamsters without any signs of aggression [2]. Injecting females with fluoxetine and thus increasing neural serotonin levels did not affect any of our measures of female sexual behavior toward heterospecific males.

The reason we used fluoxetine is that previous studies in rats reported a decrease in female sexual behavior after injection of this drug [7–9,14–16]. We predicted that a similar decrease in sexual behavior in female Syrian hamsters might lead to discrimination against heterospecific males. However, we observed no decrease in receptivity in female Syrian hamsters in response to a single dose of fluoxetine as has been reported in rats. It should be noted, however, that even different strains of laboratory rats respond differently to fluoxetine [16].

It is not clear why in our study fluoxetine did not decrease latency or duration of lordosis towards conspecific or heterospecific males. In a previous study on Syrian hamsters it was found that 10 mg / kg of fluoxetine decreased lateral displacement [12]. No measure of lordosis was recorded in that study. Thus it is difficult to draw comparisons between that study and ours. However, it is possible that whereas one dose of fluoxetine does not influence the latency and duration of lordosis, such treatment may affect aspects of the lordotic behavior (e.g., lateral displacement).

In the original study by Murphy (1978), female Turkish hamsters attacked heterospecific males but mated with conspecific males in most cases. The lack of this finding in the current study could be due to a general decrease in aggressiveness that occurs during domestication in laboratory stocks, which in turn may be due to preferential use of less aggressive animals for mating in laboratory colonies due to ease of handling [3]. In laboratory stocks of Syrian hamsters, females are less aggressive when receptive than on other days of the estrous cycle [17]. We do not know whether estrous Syrian hamsters in the wild are more aggressive than the captive stocks. However, captivity normally leads to a decrease in agonistic behavior [3]. In the case of estrous female Syrian hamsters, such a decrease in aggressiveness may have led to a corresponding decrease in discrimination against heterospecific males. If so, altering the aggressiveness of estrous females by use of drugs might cause them to be more aggressive to heterospecific males and thus also less receptive to them. This could be done by decreasing levels of serotonin or increasing levels of vasopressin [4,18].

We did find that females displayed lordosis faster and longer in the presence of a conspecific male. However, these differences in lordosis latency and lordosis duration between the conspecific and heterospecific conditions, even though statistically significant, were small (see Fig. 1 and Fig. 2). More biologically relevant is that females mated with heterospecific males in all trials and that females did not show any sign of aggression toward heterospecific males.

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Figure 1.

Latency to display lordosis when female Syrian hamsters were injected with vehicle or fluoxetine and then sequentially paired with a conspecific male and a heterospecific male (Turkish hamster). Values represent mean $\pm$ SD. **, $P < 0.01$. NS denotes a statistically non-significant difference between vehicle and fluoxetine treatments while controlling for differences between conspecific and heterospecific conditions.

Figure 2.

Duration of lordosis when female Syrian hamsters were injected with vehicle or fluoxetine and then sequentially paired with a conspecific male and a heterospecific male (Turkish hamster). Values represent mean $\pm$ SD. ***, $P < 0.001$. NS denotes a statistically non-significant difference between vehicle and fluoxetine treatments while controlling for differences between conspecific and heterospecific conditions.