Central Effects of Yohimbine on Copulatory Behavior in Aged Male Rats

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It is well known that yohimbine has a history of popular use because of its supposed aphrodisiac properties. The present study was done to determine whether yohimbine can modify the copulatory behavior of aged male rats. Adult male rats of the Wistar-Imamichi strain, 52 weeks of age and weighing 600-650g, were injected intracerebroventricularly with yohimbine hydrochloride (5, 10 µg/10 µl/rat) or vehicle. Each male was then given the opportunity to mate with a receptive female for 30 min after administration of yohimbine or vehicle. Yohimbine produced significant decreases in the latency to initial mounting and significant increases in the number of mountings. However, there was no ejaculation in the yohimbine- and vehicle-treated males. This study is the first to clearly establish an important modulator of sexual arousal for yohimbine in aged male rats. — KEY WORDS: aging, copulation, male rat, yohimbine

Materials and Methods

Animals: Sexually experienced male rats of the Wistar-Imamichi strain (Imamichi Institute for Animal Reproduction, Omiya, Saitama 330, Japan), approximately 12 (young adult) and 52 (aged adult) weeks old at the start of the experiments, were used. The animals were kept in a room with a temperature of 22-27°C.
and subjected to a light-schedule of 14 hrs light and 10 hrs darkness (light off at 19:00). They were provided with pellet diet GB-1 (Funabashi Farm Co., Ltd., Funabashi, Chiba 273, Japan) and water ad libitum. Stimulus females of the same strain were rendered sexually receptive by treatment with estradiol benzoate and progesterone before exposure to males.

Surgery: For intracerebroventricular (i.c.v.) administration 2 days before the experiments, the animals were anesthetized with nembutal (40mg/kg, i.p.) and implanted with a guide cannula 0.4mm in diameter in the right lateral ventricle according to the coordinates indicated by a stereotaxic atlas [11] (1.0 mm behind the bregma, 1.0 mm lateral to the midline, and 4.0mm below the skull). The cannulae were secured to the skull with acrylic dental cement. Rats were individually housed after i.c.v. cannulation. To determine whether the cannula was completely inserted into the right lateral ventricle, each male was sacrificed for gross examination at the end of testing. If injections were localized outside the defined regions the results concerned were omitted from the data analyses.

Drugs: Yohimbine hydrochloride was obtained commercially from Sigma Chemical. On the day of testing, the drug dissolved in distilled water was injected into i.c.v. in a volume of 10 µl per rat via an internal cannula. Control males were given the same volumes of distilled water.

Copulatory behavior: After a male rat was placed in the semi-circular observation cage (radius 40, height 50 cm) faced with Plexiglass under low-level red-light illumination for a few minutes, yohimbine (1, 5 and 10 µg/rat) was administered i.c.v. to the male and then immediately a sexually receptive female was introduced to its cage. Tests lasted 30 min from the introduction of the female. Behavioral testing was conducted between 19:30 and 21:30. The behavior categories scored included the following [5]. Mounting frequency: number of mounts without intromission preceding ejaculation. Intromission frequency: number of mounts with intromission preceding ejaculation. Ejaculation frequency: number of ejaculations during 30 min. Mount latency: time from the presentation of female to the male’s first mount. Intromission latency: time from the presentation of the female to the male’s first intromission. Ejaculation latency: latency from the first intromission until ejaculation. Post-ejaculatory interval: latency from ejaculation to the next intromission.

Locomotor activity: The spontaneous motor activity monitor for small animals of Saito et al. [13] was used. The monitor was designed to measure animal ambulation along a horizontal axis by means of two infrared photo-beams. An open field of 40 cm in diameter and 38 cm in height was used. The experimental rat was placed gently in the center of the open field immediately after the drug administration. The measured value during 30 min after the treatment was taken as the locomotor activity. The dosage of yohimbine was 10 µg per rat.

Statistics: Behavioral frequencies and latencies were analyzed using the Mann-Whitney U test for independent comparisons of groups [9].

Results

Copulatory behavior: As shown in Fig. 1, the median (and range) numbers of mount, intromission and ejaculation during 30 min in young adults were 23 (8-44), 17 (7-32) and 1 (1-3), respectively. Aged adults showed only mounting behavior and its median number was 6 (0-11). There were significant differences in the numbers between young and aged adult groups (p < 0.01). The median latency to first mount was significantly shorter for the young adults, compared with the aged adults (266 versus 882 sec, p < 0.01, Fig. 2).

Administration of yohimbine to aged adult rats altered mounting frequency and mount latency. Yohimbine at the 5 and 10 µg/rat dose significantly increased the number of mounts and decreased the latency to the first mount, compared with the distilled water-injected control (p < 0.05-0.01, Figs. 3, 4). These values were similar to those in young adult rats. There were no changes in the parameters other than those above.

Locomotor activity: The spontaneous activities during 30 min after administration of yohimbine and vehicle were 11 (0-73) and 62 (54-104), respectively (Fig. 5). There was a significant difference in the locomotor activity between the two groups (p < 0.05).
Fig. 1. Copulatory behavior of aged adult rats (n=6), compared with young adults (n=6). M=mounting I=intromission E=ejaculation. **Significantly different from the respective young adults (p <0.01).

Fig. 2. The initial delay in mounting by aged adult rats (n=6), compared with young adults (n=6). **Significantly different from young adults (p <0.01).

Fig. 3. Effects of yohimbine on the number of mounts in aged adult rats (n=21, separated into three equal doses and n=7 for yohimbine- and vehicle-treated males, respectively). *p <0.05 **p <0.01 vs. control.

Fig. 4. Effects of yohimbine on the latency to initial mounting in aged adult rats (n=21, separated into three equal doses and n=7 for yohimbine- and vehicle-treated males, respectively). *p <0.05 **p <0.01 vs. control.
Discussion

Three findings of our study were as follows: 1) the copulatory behavior in aged adult rats compared with the young adults was significantly defective in the numbers of mounting, intromission and ejaculation, and the latency to first mount; 2) when yohimbine was given intracerebroventricularly, the aged adults exhibited more mounts and shorter mount latency while they showed neither intromission nor ejaculation during 30 min, compared with the vehicle controls; 3) despite the increasing mounting behavior in yohimbine-treated aged adults, the locomotor activity was suppressed. Testing of 30 min may be inadequate when studying the capacity of the copulatory behavior of the aged adult rats. If given the test of copulatory behavior during more than 30 min, they do have intromission and ejaculation behaviors. However, it is true that the response latency was prolonged in aged adults. While the young males started to copulate as soon as the receptive females were presented to them, the aged adults had significantly increased latency before initially copulating. The young adults seem to be more easily aroused than the aged adults. This may indicate that the threshold in aged adults for the arousal of the copulatory response is very high, compared with young adults.

Yohimbine, a potent \(\alpha_2\)-adrenoceptor antagonist, facilitates norepinephrine release from the presynaptic neurons or inactivates the postsynaptic \(\alpha_2\)-receptors in the postsynaptic neurons \([3,10]\). Yohimbine given i. p. is remarkably effective in young adult male rats in stimulating certain aspects of sex behavior \([2]\). When aged adult rats were injected with yohimbine, the sexual arousal was facilitated the same as in young adults. However we observed no intromission or ejaculation behaviors in aged adults. Humphries et al. \([6]\) reported that \(p\)-chloroamphetamine (PCA), releasing central 5-hydroxytryptamine (5-HT) from serotonergic nerve terminals, induced ejaculation in rats. It appeared that 5-HT played some part in this effect. It seems that serotonergic systems play a role in control of ejaculation. Thus, central nervous systems may be different for sexual arousal and ejaculation. Perhaps the ejaculation in aged adults is induced by PCA. On the other hand, it is interesting that locomotor activity was suppressed by yohimbine at the dose of 10 \(\mu g/rat\). Chopin et al. \([1]\) also demonstrated that yohimbine-treated rats showed significantly less locomotor activity than the control animals. These results indicate that yohimbine apparently stimulates the essential component of sexual activity and suppresses locomotor activities. These effects of yohimbine on sexual and locomotor activities seems paradoxical.

These data are the first to show that yohimbine is an important modulator of sexual arousal in aged adult rats. Further study may lead to developments in the pharmacological treatment of sexual dysfunction.

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References

COPULATION IN AGING RATS BY YOHIMBINE


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高齢ラットの交尾行動に対するヨヒンピンの中枢効果について

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生後52週齢の成熟雄ラットに古くから催情剤として使用されてきたヨヒンピン（5, 10 \( \mu \)g/rat）を側頭室に投与し、その後30分間の交尾行動を観察した。その結果、ヨヒンピン投与群は各個体群間で比較してマウント潜時の有意な減少（p < 0.01）およびマウント回数の有意な增加（p < 0.01）が観察された。しかし、イントロミッションおよび射精は観察されなかった。一方、ヨヒンピン投与群（10 \( \mu \)g/rat）の自発運動量は対照群に比較して有意な減少を示した（p < 0.05）。以上の成績より、ヨヒンピンは高齢ラットに対しても性的興奮の調節機構に関与しているものと推測される。