—Note—

Effects of Naloxone and Naltrexone on Receptive and Proceptive Behaviors in Female Rats

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The sexual receptive and proceptive behaviors induced by opiate antagonists, naloxone and naltrexone in estrogen-primed ovariectomized rats were observed under the presence of sexually active males. The females were treated intraperitoneally with naloxone or naltrexone at doses ranging from 0.5 to 4.0 mg/kg and the sexual behavior of females was tested before and after the injection of drug. The results obtained suggest that the opiate antagonists play a role in the regulation of lordosis behavior, but not proceptive behavior in female rats. —KEY WORDS : female rat, opiate antagonist, sexual behavior

The deleterious effects of opioids on human sexuality have long been recognized. For example, loss of libido and sexual potency typically follows chronic use of opiate drugs [1]. Studies in laboratory animals support these findings. In male rats, administrations of β -endorphin [4] or morphine [3] impair copulatory performance. Conversely, the opiate receptor blocker naloxone hydrochloride induces mating in sexually inactive male rats [2], and facilitates sexual performance in copulating male rats [5]. The role of opiates in the regulation of female sexual behavior is less clear.

The purpose of the present study is to determine whether sexually inactive female rats peripherally injected with opiate antagonists, such as naloxone and naltrexone would facilitate receptive and proceptive behaviors.

Animals : Sixty-four mature female rats of Wistar-Imamichi strain (Imamichi Institute for Animal Reproduction, Tsuchiura) were used. The animals were kept under controlled light (14 hr light, 10 hr dark ; lights off at 19 :

00) and temperature (22–27°C) conditions. They received a standard laboratory diet (MB-1, Funabashi Farm Co. Ltd., Chiba) and tap water *ad libitum*. At approximately ten weeks of age, animals were bilaterally ovariectomized under ether anesthesia. Two weeks later, all female rats received estradiol benzoate (20 μ g/rat, S. C.), dissolved in 0.1 ml sesame oil, 48 hours before exposure to males.

Drugs : Naloxone hydrochloride and naltrexone hydrochloride (Sigma Chemical Co., St. Louis) were dissolved in 0.9% saline and administered intraperitoneally at volume of 0.1 ml/100g body weight. Control females were given the same volume of saline.

Lordosis behavior : Each female was placed in a semi-circular observation cage (radius 40 cm, height 50 cm) with a sexually active of the same strain. When tests were initiated at 19 : 00 of the dark period, dim red light was provided. The behavior of female was observed until she received a total of 10 mounts. The presence or absence of lordosis was recorded in

Fig. 1. Mean lordosis quotients prior to (blank columns) and following (filled columns) the injection of naloxone in estrogen-primed ovariectomized rats ($n=8$ for each dose). Significant levels were calculated using the Wilcoxon's signed rank test. Vertical line in each column represents $\pm$ SE.

Fig. 2. Mean lordosis quotients prior to (blank columns) and following (filled columns) the injection of naltrexone in estrogen-primed ovariectomized rats ($n=8$ for each dose). Significant levels were calculated using the Wilcoxon's signed rank test. Vertical line in each column represents $\pm$ SE.

each mount, and the results were expressed in terms of the lordosis-to-mount (L/M) ratio, used as an index of sexual receptivity. In addition, the incidence of proceptive behaviors such as earwiggling, hopping and darting was also recorded.

Experimental procedure : Sixty-four female rats preliminary tested for lordosis behavior, in the absence of drug treatment

(non-treatment), were separated into eight equivalent groups. Four groups were injected with saline or naloxone hydrochloride (0.5, 1.0 and 2.0mg/kg, I. P.) and other four groups were injected with naltrexone hydrochloride (0, 1.0, 2.0 and 4.0mg/kg, I. P.). The lordosis behavior testings before and after drug treatment were performed 30 min interval.

Statistical analysis : The L/M ratios were analyzed using the Wilcoxon's signed rank test. For comparison of incidence of behaviors, Fisher's exact probability test was used.

In the preliminary testing without drug treatment, the mean L/M ratio and incidence of proceptivity in estrogen-primed ovariectomized females were 0.14 ± 0.09 (S. E.) and 0, respectively. As shown Figs. 1 and 2, administrations of 0.5, 1.0 or 2.0 mg/kg naloxone and 1.0, 2.0 or 4.0mg/kg naltrexone resulted in a significant increase in the L/M ratios, compared with each non-treatment group ($p < 0.01$ or 0.001). These drugs showed a dose-dependent increase in the L/M ratios, while saline treatment did not alter the L/M ratios in naloxone- and naltrexone-treated groups. On the other hand, proceptive behaviors in all animals treated with both drugs were not induced.

These results indicate that peripheral administrations of opiate antagonists, naloxone and naltrexone facilitate sexual receptive behavior in sexually inactive female rats. Our findings are in agreement with those obtained with central infusions of naloxone by Sirinathsinghji [9]. It may be possible that naloxone and naltrexone penetrate into the central nervous system through the blood-brain barrier and play a role in the regulation of lordosis behavior. In addition, our data show that both drugs have no influence on proceptive behaviors. Previous studies [6, 7] have demonstrated that estrogen-primed ovariectomized female rats treated with LHRH display receptive, but not proceptive behaviors. Sirinathsinghji *et al.* [8] has described that a combination of naloxone and anti-LHRH antiserum, or LHRH antagonist analogue has no elevation of lordosis quotient. This action of naloxone on lordosis behavior may be due to the secretion of LHRH. Whereas the appearance of proceptivity does not seem related to the opiate receptor. These findings indicate that neural systems mediating the receptivity are different from those mediating the proceptivity of

sexual behavior.

In conclusion, the opiate antagonists reliably play a role in the control of sexual receptive, but not proceptive behaviors in female rats.

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雌ラットの性行動に対するナロキソン およびナロトレキシンの効果について

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エストロゲン前処置卵巢摘出成熟ラットにオピエートの拮抗薬であるナロキソン、ナロトレキシンを腹腔内に投与し、投与後の雌に対する性行動の変化（ロードーシ

スおよび勧誘行動）を観察した。その結果、ロードーシス行動の促進を認めたが、勧誘行動の発現は見られなかった。