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BRIEF COMMUNICATION

# Effects of Naloxone on Penile Erection in Cats

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DOMER, F. R., G. WESSLER, R. L. BROWN AND A. MATTHEWS. *Effects of naloxone on penile erection in cats.* PHARMACOL BIOCHEM BEHAV **30**(2) 543–545, 1988.—Male cats were anesthetized with pentobarbital. A Foley catheter was placed in the urinary bladder and physiologic saline, under a head of pressure, was allowed to flow at a constant rate through the bladder. Naloxone, 0.2 mg, caused penile erection in 5 of 11 experiments. The onset of action was 0.5 to 4 minutes, and the duration of the erection was 5 to 36 minutes. In two of three experiments a second injection of naloxone caused a second erection. The erection caused by naloxone was not changed by pre- or posttreatment with morphine or by posttreatment with propranolol. It was suggested that the erection could be due either to altered levels of hormones released from the central nervous system or to removal of reflex inhibitory tone in the spinal cord or sacral parasympathetic ganglia.

Penile erection Naloxone Anesthetized cats

THE occurrence of impotence in men and its treatment has long been of great interest. Currently a common approach being employed for the pharmacologic control of impotence is the use of an alpha adrenergic blocking agent plus papaverine injected into the corpora cavernosa [1, 12, 18]. Nevertheless, a broad variety of other compounds are known to increase the incidence of penile erection. These include imipramine [6,19], verapamil [6], apomorphine [22], naloxone or naltrexone [20,25], oxytocin [21], yohimbine [24], beta$_2$ adrenergic agonists [9], and stimulation of 5-hydroxytryptamine$_1$ receptors [3]. As our earlier work [9] had implicated the adrenergic nervous system to be of importance in the initiation and termination of penile erection, it was felt to be of interest to extend our observations to include some of the other classes of pharmacologic agents. The present observations deal with an evaluation of the effects of an agonist and an antagonist at the opioid receptor on the initiation of penile erection.

## METHOD

The methods are the same as those reported previously [9]. Male cats weighing 2.9 to 4.9 kg were anesthetized with pentobarbital sodium (35 mg/kg of body weight) injected intraperitoneally. The lower abdomen was shaved and cleaned with Betadine® solution. A midline suprapubic incision was made, the anterior rectus fascia was incised, and the rectus muscle was separated bluntly exposing the retropubic space. The anterior surface of the bladder was then exposed and cleared of perivesicular fat, a purse-string suture was placed on the anterior wall of the bladder, and a No. 8 French Foley catheter was introduced through a stab incision. The left or right groin was prepared in a sterile fashion, the femoral artery and vein were dissected and cannulated with a No. 23 or No. 25 butterfly-type needle to permit monitoring of the blood pressure and to permit administration of medications, respectively.

The cannula in the femoral artery was connected to a Statham P23 transducer attached to a Grass Model 7 Polygraph for the recording of the blood pressure. The bladder catheter was connected to a reservoir containing a sterile solution of 0.9 percent sodium chloride injection, U.S.P. (Travenol). The height of the reservoir was adjusted until the pressure caused a continuous flow per urethra. Once the urinary flow was established, drugs were administered intravenously and the effect of penile erection assessed. When penile erection occurred the length of the penis was measured using a small centimeter ruler at variable intervals of time until the effect wore off. The procedure was terminated after the experimental studies by removing the Foley catheter. The wound was then closed in a routine fashion around a small Penrose drain placed over the bladder. The groin incision was closed after the removal of both cannulae. Neosporin powder was placed on the incision, and the animal was returned to the Vivarium for use at intervals of not less than 7 days. Drugs and doses (as the salts) used in these experiments were: naloxone hydrochloride (0.2 mg), terbutaline sulfate (0.5 mg/kg), morphine sulfate (1 mg/kg), and propranolol hydrochloride (0.5 mg/kg).

TABLE 1

EFFECT OF NALOXONE (0.2 mg) ON PENILE ERECTION IN CATS

| Experiment No. | Cat No. | Penile Erection + | Penile Erection − | Latency (min) | Duration (min) | Remarks |
|---|---|---|---|---|---|---|
| 1 | 1 | + | | 1 | 8 | |
| 2 | 1 | | − | | | |
| 3 | 2 | + | | 4 | 36 | no erection when flow stopped; retching |
| 4 | 2 | + | | 0.5 | 14 | |
| 5 | 2 | | − | | | |
| 6 | 2 | | − | | | |
| 7 | 2 | | − | | | retching |
| 8 | 3 | + | | 2 | 5 | |
| 9 | 3 | | − | | | erection with terbutaline |
| 10 | 4 | + | | 1 | 12 | no erection when flow stopped; retching |
| 11 | 4 | | − | | | erection with terutaline |

## RESULTS

A total of eleven experiments were performed with naloxone in 4 cats which were found to be capable of penile erection at least once (Table 1). In 5 instances administration of naloxone resulted in penile erection, whereas in 6 others there was no such response (i.e., a 45% positive response). However, three other animals did not respond to naloxone, terbutaline, or phentolamine and were presumed to have an erectile dysfunction.

In two of three experiments in which naloxone caused penile erection, a second injection caused an erection a second time. In both of these experiments, administration of morphine did not cause a noticeable change in the intensity or duration of the erection. Additionally, administration of propranolol during an erection did not cause a noticeable change in the intensity or duration of the erection.

Although the administration of naloxone caused no change in the blood pressure, some minutes after its administration retching occurred in three of the experiments.

Peripheral stimulation must be involved in the penile erection because cessation of the perfusion of the bladder caused the penis to detumesce in two experiments and to recur when the flow was initiated again.

## DISCUSSION

Opioid agonists inhibit gonadotropin-releasing hormone leading to a decrease in the concentration of testosterone in the circulation while increasing the release of prolactin, growth hormone, adrenocorticotrophic hormone, and vasopressin [5, 7, 8, 11, 15, 17, 28–30]. Naloxone, an antagonist at the opioid receptor, has been found to block or reverse these effects in many studies [5, 7, 8, 11, 13, 15, 17, 23, 28–30]. The resultant increase in testosterone and decrease in prolactin in the circulation may underlie the processes involved in penile erection. Additionally, naloxone has been found to increase the release of oxytocin from the neurohypophysis [2,4]. The receptors involved in these changes may be dopaminergic in type in that apomorphine will cause penile erection [27], and this compound is known to stimulate dopaminergic receptors [16]. Apomorphine is employed as an emetic. In three of the present experiments the cats retched following the administration of the naloxone. The pairing of events suggests a possible common class of receptors may be involved in emesis and penile erection. Neuroleptics, which are known to block dopaminergic receptors, have been reported to cause impotence in men with psychiatric problems [14].

In two of the present experiments penile erection following administration of naloxone likely involved a peripheral component as was indicated by the observed dependence of maintaining the erection on urinary flow. This would suggest the activity in the bladder itself or in the neurons in the spinal cord could be affected by naloxone. Naloxone has been reported to excite nociceptive neurons in the feline spinal cord [15] and to remove chronic inhibitory tone in the spinal cord or in parasympathetic ganglia leading to the urinary bladder [10,26]. Activation of the parasympathetic nervous supply to the genitourinary system may explain why propranolol did not block the penile erection caused by naloxone as it had previously in our experiments that involved $beta_2$ adrenoceptors [9]. As we were unable to cause penile erection in over half of the present experiments with naloxone, and phentolamine, terbutaline, and naloxone did not cause penile erections in three other cats, there must be multiple means for activating this reflex.

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