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Naloxone Suppresses Feeding and Drinking but not Wheel Running in Rats[1]

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CAREY, M. P., J. A ROSS AND M. P. ENNS *Naloxone suppresses feeding and drinking but not wheel running in rats* PHARMAC BIOCHEM. BEHAV 14(4)569–571, 1981 —The effects of naloxone hydrochloride on food and water intake and number of wheel revolutions were measured in male rats The administration of 10 mg/kg naloxone but not 1 mg/kg suppressed the 3-hr food and water intake in nondeprived rats Naloxone injections (1 mg/kg or 10 mg/kg) were ineffective in altering the number of wheel revolutions in nondeprived or food deprived rats These results support the interpretation that the suppressive effects of naloxone previously reported with deprived rats are evident in nondeprived rats and are specific to feeding and drinking.

Naloxone Food intake Water intake Activity

RECENT research has indicated that naloxone suppresses food and water intake. A single administration of a small dose of naloxone (1 mg/kg) suppresses the food intake of both lean [3,8] and genetically obese [12] food-deprived rats and mice and the water intake of water-deprived rats and mice [3,8]. This suppression does not indicate, however, whether the pharmacological agent is altering a physiological state associated with feeding and drinking or even whether it is specific to these behaviors [9,10]. Additionally, the measurement of food and water intake of deprived animals confounds the action of the pharmacological agent with the nutritional status of the animal [1].

The purpose of this experiment was to determine whether the suppressive effects of naloxone are specific to feeding and drinking by examining simultaneously activity levels and food and water intake of rats maintained ad lib and by examining activity levels of food-deprived rats.

METHOD

Subjects

The subjects were 21 experimentally naive, 120-day old, male, Long-Evans rats weighing 400–450 g at the onset of testing (Blue Spruce Farms, Inc., Altamont, N.Y.). The rats were individually housed in running wheels with attached cages (Wahmann LC 34) in a temperature (72°F±2°F) and humidity (55%±2%) controlled colony, illuminated between 0400 and 1600 hours.

Procedure

Rats, maintained on ad lib food (Charles River Rat Chow Pellets) and water, were acclimated to the wheels and cages (days 1–20), matched according to the number of wheel revolutions in 24 hours, then assigned randomly to one of three groups. Group I received injections of isotonic saline (1 ml/kg). Group II received 1 mg/kg injections of naloxone HCl (Endo Laboratories, Garden City, N.Y.) and Group III received 10 mg/kg injections of naloxone HCl. All doses of naloxone were expressed in terms of salt base, were dissolved in isotonic saline, and were volumetrically equal (1 ml/kg).

The rats were given six intraperitoneal (IP) injections, each separated by a 48-hr interval (days 21, 23, 25, 27, 29, 31). All injections were given at the onset of the dark cycle. Food intake (±0.1 g), water intake (±0.2 ml) and number of wheel revolutions were measured separately for the first 3 hours and the last 21 hours of each of the last 6 days of the acclimation period (baseline), the 6 injection days (treatment), and the 6 one-day intervals which separated the injection days (recovery). Comparisons of the 3-hr and the 24-hr food intake, water intake and number of wheel revolutions (logarithmic transformations) were made using two factor analysis of variance with repeated measures on one factor and Neuman-Keuls tests. Changes across conditions (baseline, treatment, recovery: 6-day means) for the three groups (saline, low dose, high dose) and changes across the six injection days (treatment) for the three groups were analyzed separately

Following this initial test period, the rats were maintained in individual cages with ad lib food and water for 21 days. On each of the following 14 days, the rats were allowed to run in activity wheels with attached cages during the first three hours of the dark cycle. After this 3-hr period, wheel revolutions and body weights were recorded and the rats were returned to the laboratory cages. Days 1–6 were baseline

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days (food and water were available ad lib). Days 7–14 were treatment days (food was completely withheld while water was available ad lib). On each treatment day, immediately prior to placement in the wheels, each rat received an injection identical to that received previously. The number of wheel revolutions (logarithmic transformations) for the 3 groups at 100, 90, and 80% body weights were analyzed using a two factor analysis of variance with repeated measures on one factor and Neuman-Keuls tests.

RESULTS

Three-hour measures, ad lib. On the baseline days, the food and water intakes of the three groups were similar. In comparison with intakes on baseline days, only the high dose of naloxone (10 mg/kg) was effective in reducing food and/or water intake (Food Intake: Groups, $F(2,18)=3.99$, $p<0.05$; Groups×Conditions, $F(4,36)=3.43$, $p<0.05$; Water Intake: Groups, $F(2,18)=12.43$, $p<0.05$; Groups×Conditions, $F(4,36)=6.34$, $p<0.05$) (see Table 1A and 1B). On the recovery days, the food and water intakes of the three groups were again similar to each other and to the intakes on baseline days.

In comparison with intakes of saline controls, both the low dose and the high dose of naloxone were effective in reducing food intake (Groups $F(2,18)=9.66$, $p<0.05$). The apparent reduction with rats given the low dose, however, is primarily a result of an increase in food intake by saline controls (see Table 1A).

On the baseline days, the number of wheel revolutions of the three groups was similar. In comparison with wheel revolution on baseline days, neither dose of naloxone was effective in altering the number of revolutions (see Table 1C). In addition, number of revolutions remained constant across the six days of injection (treatment).

Twenty-four-hour measures, ad lib Naloxone (1 mg/kg or 10 mg/kg) did not alter 24-hour measurements of feeding, drinking or wheel running.

Three-hour measures, food deprivation On the subsequent baseline days, the number of wheel revolutions of the three groups was again similar. The number of wheel revolutions increased with the severity of food deprivation for each of the three groups (deprivation $F(2,36)=4.32$, $p<0.05$). There were no reliable differences in wheel revolutions between groups at either level of deprivation (see Table 2).

TABLE 1

MEAN (SEM) 3-HR FOOD INTAKE, WATER INTAKE, AND WHEEL REVOLUTIONS FOR BASELINE, TREATMENT, AND RECOVERY CONDITIONS

	Baseline	Treatment	Recovery
A. Food Intake (grams)			
Isotonic saline	3 2 (0.4)	3.8 (0.4)	3 0(0 4)
Naloxone (1 mg/kg)	2 8 (0 3)	2 7 (0.3)	3 2(0 2)
Naloxone (10 mg/kg)	2.6 (0.2)	1 7 (0 3)	2.9(0 4)
B Water Intake (milliliters)			
Isotonic saline	5 2 (0 7)	4.9 (1 2)	4 3(0 7)
Naloxone (1 mg/kg)	5.6 (0 6)	4.6 (0 9)	6 1(0.7)
Naloxone (10 mg/kg)	4.8 (0 5)	1.1 (0.3)	3 8(0 8)
C. Wheel Revolutions (Antilog of the mean)			
Isotonic saline	36 3(14 9)	45 7(14 8)	20 9(9 2)
Naloxone (1 mg/kg)	33 9(13 9)	38 0 (6.4)	32 4(6 7)
Naloxone (10 mg/kg)	25.1(14.6)	26 3 (8 9)	24 5(9 0)

During the treatment condition each group received an IP injection of either isotonic saline, 1 mg/kg naloxone, or 10 mg/kg naloxone immediately preceding the 3-hr period Each number represents the mean performance over six days

TABLE 2

ANTILOG MEAN (SEM) 3-HR WHEEL REVOLUTIONS AT 100, 90, AND 80 PERCENT BODY WEIGHT FOR RATS GIVEN ISOTONIC SALINE, 1 mg/kg NALOXONE, OR 10 mg/kg NALOXONE

	Percent Body Weight		
	100	90	80
Isotonic saline	95 1 (30 8)	104 3 (28 3)	194 0 (77 5)
Naloxone (1 mg/kg)	80.7 (16 1)	72 2 (25 1)	154 4 (66 8)
Naloxone (10 mg/kg)	98 9 (29 3)	131.1 (64 0)	172 1 (92 5)

DISCUSSION

Naloxone (10 mg/kg) suppressed feeding and drinking in rats given ad lib food and water. This suppression was obtained following the initial administration, remained constant with repeated injections, and was temporary. There was no suppression when feeding or drinking was measured 24 hours following the injection nor on the recovery days which separated the days of injection These data are similar to those obtained with nondeprived and deprived rats and mice [2, 3, 8, 14].

In comparison with baseline measures, the low dose of naloxone (1 mg/kg) did not reliably reduce 3-hr food or water intakes. It is possible that this dose is only effective during the first one or two hours following the injection [12]. It is also possible that this dose, while effective with deprived rats, is not effective with rats fed ad lib [13].

Wheel running was not reliably altered following either the 1 mg/kg or the 10 mg/kg injections of naloxone in either rats fed ad lib or in rats deprived of food. These results are consistent with measures of locomotor [11] and shuttlebox [7] activity following 1–10 mg/kg injections of naloxone and support the interpretation that the suppressive effects of naloxone are specific to feeding and drinking [12]

Numerous studies have demonstrated that wheel running increases with deprivation (see [5]), and it has been suggested that this increase alters physiological states associated with the deprivation. However, several studies which manipulated these states have failed to find relationships between the manipulations and wheel running activity (see [4,6]). Data from this experiment also failed to find relationships between ingestive behaviors and wheel running activities, further suggesting a dissociation between mechanisms controlling food and water intake and mechanisms controlling activity levels.

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