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BRIEF COMMUNICATION

Morphine Conditioned Place Preference in the Hamster

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SCHNUR, P. AND J. MORRELL. *Morphine conditioned place preference in the hamster.* PHARMACOL BIOCHEM BEHAV **37**(2) 383–385, 1990.—Two experiments investigated the ability of morphine to produce a conditioned place preference in the hamster. In Experiment 1, it was found that a 15 mg/kg dose of morphine produced a conditioned place preference after eight conditioning trials. In addition, naloxone (0.4 mg/kg blocked the development of the morphine-conditioned place preference and itself produced a conditioned place aversion after four conditioning trials. In Experiment 2, the effects of four doses of morphine (0, 2.5, 5 and 15 mg/kg) on the acquisition of a conditioned place preference were studied. Only the 15 mg/kg dose produced a significant place preference. Compared to similar findings in the rat, the present results indicate that a relatively high dose of morphine is required to produce a conditioned place preference in the hamster.

Morphine Naloxone Conditioned Place preference Hamster

CONDITIONED place preference procedures have been employed widely to identify the affective properties associated with drug administration (1, 4–8, 10, 15). Rats show conditioned place preferences for environments associated with morphine and conditioned place aversions for environments associated with the opiate antagonist, naloxone (1, 4–8, 10, 15). The purpose of the present experiments was to investigate the effects of morphine on conditioned place preference in the hamster.

METHOD

Subjects

The subjects were female golden Syrian hamsters, *Mesocricetus auratus*, obtained from Sasco, Inc. (Omaha, NE) and weighing approximately 133 g. They were housed singly in hanging stainless steel cages with free access to tap water, Purina lab chow and paper nesting materials. They were maintained on a 12:12 hr light-dark cycle (lights on at 0700) in a temperature-controlled vivarium. All experiments were conducted during the light phase. Twenty subjects were used in each of the experiments reported below.

Apparatus

The apparatus consisted of two identical Plexiglas shuttleboxes. Each box had two compartments ($20 \times 11.5 \times 20.5$ cm) connected by a central holding area ($12 \times 11.5 \times 20.5$ cm). One compartment had white walls and ceiling, a smooth masonite floor and a small illuminated lamp (28 V) mounted at the top of one wall. The other compartment had black walls and ceiling, a grid floor and no lamp. Matching white and black guillotine partitions sealed off the compartments from the central holding area. Photocells in each compartment were used to detect an animal's position in the box and solid-state timers were used to record the amount of time spent in each end compartment. Extraneous sounds in the laboratory were masked by a noise source that maintained an ambient level of 76 dB SPL.

Procedure

Experiment 1. During the first five days of the experiment, each hamster's initial preference for the white or black side of the apparatus was determined. The hamster was placed into the central holding area for a few seconds until the guillotine doors were simultaneously removed giving the animal free access to both chambers for 15 min. The time spent on either side was measured. Time spent in the holding area was not recorded. Results of these initial tests indicated no strong preferences for either side of the shuttlebox. Therefore, animals were assigned randomly to one of four groups ($n = 5$) for the conditioning stage of the experiment. During the next four days, each group received two daily injections 10 min apart before being placed in one randomly chosen side of the apparatus for 40 min. Across all groups, equal numbers of subjects were conditioned in the white and black sides of the apparatus. Group SAL/SAL received two saline injections; Group SAL/MS received saline in the first injection, followed by morphine in the second injection; Group NLX/SAL received naloxone followed by saline; Group NLX/MS received naloxone followed by morphine. After four days of conditioning, animals were tested as follows: All hamsters were given an injection of saline, placed in the central holding area for a few seconds and simultaneously

allowed free access to both sides of the shuttlebox for 15 min. Time spent in either side was measured. Four additional days of conditioning followed and then a second test, conducted exactly as the first, was given. Morphine injections consisted of a 15 mg/kg dose of morphine sulfate. Naloxone hydrochloride was given in a 0.4 mg/kg dose. Doses are expressed as the salt. Saline injections were 0.9% sodium chloride. All injections were administered SC in the dorsal surface of the neck in 1 ml/kg volumes.

Experiment 2. Initial preference testing was carried out as in Experiment 1 and, since no strong preferences were revealed, animals were assigned randomly (n=5) to receive one of four doses of morphine [0(saline), 2.5, 5, 15 mg/kg]. During the next eight days, animals were given an injection of a dose of morphine and confined to one or another side of the shuttlebox for 40 min. On Day 9, animals were tested as in Experiment 1. In other respects, the procedures of the two experiments were identical.

RESULTS

Experiment 1

Figure 1 (top) shows the percent of time that subjects spent on the drug-associated side of the shuttlebox during the first test session for all groups. A 2 (First Injection) × 2 (Second Injection) factorial analysis of variance (ANOVA) indicated that the effect of the first injection was significant, $F(1,16)=21.31$, $p<0.001$. That is, animals given naloxone in the first injection spent less time on the drug-associated side than did animals given saline. No other effects were significant.

Figure 1 (bottom) shows the percent of time that subjects spent on the drug-associated side during the second test session for all groups. A 2 (First Injection) × 2 (Second Injection) factorial ANOVA indicated that the effects of the first injection, $F(1,16)=19.00$, $p<0.001$, the second injection, $F(1,16)=6.08$, $p<0.02$, and the interaction, $F(1,16)=9.64$, $p<0.01$, were significant. Further analysis of the interaction using Tukey's HSD Test (Kirk, 1986) indicated that the difference between Group SAL/SAL and Group SAL/MS was significant ($p<0.05$), that the difference between Group SAL/MS and Group NLX/MS was significant ($p<0.05$), but that the difference between Group SAL/SAL and Group NLX/SAL was not. Thus, animals given morphine in the second injection spent more time on the drug associated side than animals given saline (Group SAL/MS vs. Group SAL/SAL), unless the morphine injection had been preceded by a naloxone injection (Group NLX/MS vs. Group SAL/MS).

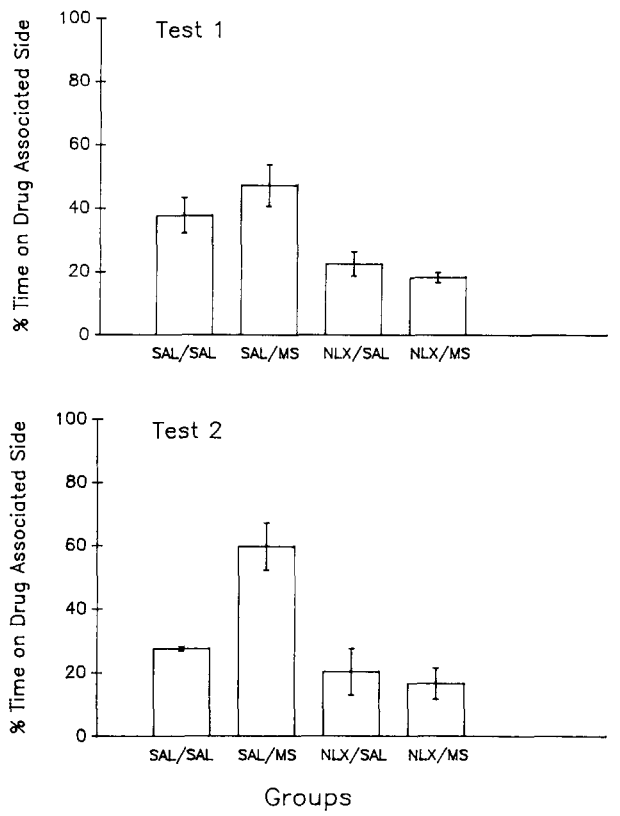

FIG. 1. (Top) Mean percent time on the drug associated side during the first test session for all groups in Experiment 1. (Bottom) Mean percent time on the drug associated side during the second test session for all groups in Experiment 1.

Experiment 2

Figure 2 shows the percent of time subjects spent on the drug-associated side as a function of the dose of morphine. A one-way ANOVA indicated that the effect of dose was significant, $F(3,16)=4.06$, $p<0.025$. Tukey's HSD Test indicated that the difference between the 15 mg/kg dose and saline controls was significant ($p<0.05$). No other differences were significant. Thus, a dose of 15 mg/kg produced a conditioned place preference in the hamster.

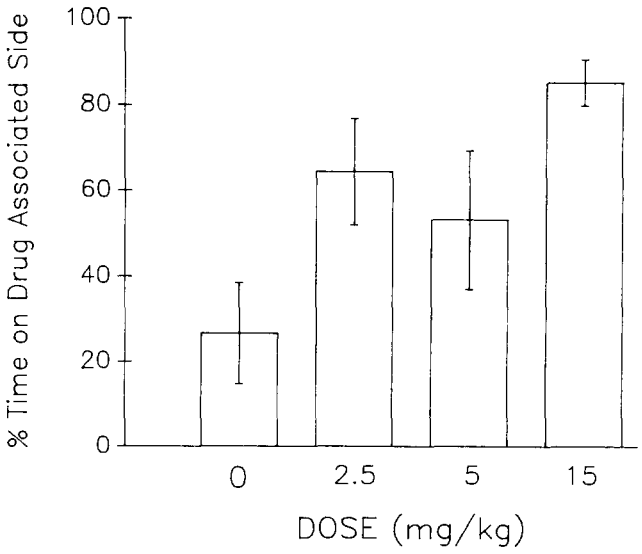

FIG. 2. Mean percent time on the drug associated side as a function of morphine dose in Experiment 2.

DISCUSSION

The results of the present experiments indicate that morphine can produce a conditioned place preference in the hamster. However, it appears that the hamster is less sensitive than the rat to the positive incentive effects of morphine (1, 6, 10, 15). In Experiment 1, a conditioned place preference was detectable only after eight conditioning trials. In Experiment 2, a relatively high dose of morphine (15 mg/kg, SC) was required to produce a significant place preference. In the rat, conditioned place prefer-

ences have been reported with SC doses as low as 0.2 mg/kg after three conditioning trials (6). Whether this represents a difference in the sensitivity of rats and hamsters to the reinforcing effects of morphine or a difference in procedures between the present experiment and those using rats will be determined by future research. Nevertheless, the present results are consistent with other research documenting the relative insensitivity of the hamster to both the sedative (2, 3, 16) and the locomotor (9,12) effects of morphine.

The present results also suggest that naloxone produces a conditioned place aversion in the hamster, as it does in the rat (6,7). This aversion was short-lived, however, appearing after four but not after eight conditioning trials in Experiment 1. In the rat, a naloxone place aversion has been reported to increase between one and four conditioning trials (6). This, too, might reflect a difference in the response of rats and hamsters to the aversive effects of naloxone. Perhaps, in the hamster, tolerance develops to the aversive effects of naloxone after the initial conditioning. Although a higher dose of naloxone might have produced a stronger aversion, it should be noted that the dose employed has been shown to antagonize morphine's biphasic effects on locomotor activity in the hamster (11, 13, 14).

In Experiment 1, animals given naloxone prior to morphine did not develop a preference for the morphine-associated place. Since naloxone produced a place aversion on the first test trial in Experiment 1, caution must be exercised in concluding that naloxone antagonized the development of the morphine conditioned place preference. Yet, that conclusion seems warranted by the finding that, on the second test trial, naloxone antagonized the morphine place preference (Group NLX/MS vs. Group SAL/MS), but did not itself produce an aversion (Group NLX/SAL vs. Group SAL/SAL).

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