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The Effect of Housing and Gender on Morphine Self-Administration in Rats

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Abstract. To determine the effect of housing conditions on morphine self-administration, rats isolated in standard laboratory cages and rats living socially in a large open box (8.8 m^2) were given morphine in solution (0.5 mg/ml) as their only source of fluid for 57 days. They were then exposed to a series of 3-day cycles previously shown by Nichols et al. (1956) to increase self-administration of morphine in caged rats. On morphine/water choice days late in the period of forced consumption, between the Nichols cycles, and during a subsequent period of abstinence, the isolated rats drank significantly more morphine solution than the social rats, and the females drank significantly more morphine solution than the males. During the four choice days in the Nichols Cycle Period the isolated rats increased their consumption, but the socially housed animals decreased theirs.

Key words: Morphine – Self-administration – Environment

Rats that have been administered morphine for a prolonged period will, under appropriate conditions, drink morphine solution when water is also available (e.g., Nichols et al., 1956; Stolerman and Kumar, 1970; Khavari and Risner, 1973; Ternes, 1975). Such studies have been cited in support of both conditioning theories of addiction (Nichols, 1965; Goldstein, 1972) and theories that explain addiction as a consequence of persistent neurochemical change (Dole, 1972).

There are, however, reasons to suspect that laboratory housing conditions might have enhanced morphine consumption in these studies. Rats in oral self-administration studies are usually tested in small, solitary metal cages. This type of housing may well be aversive to rats, which are normally gregarious, wide-ranging, and curious animals (Lore and Flannelly, 1977). Since opiates are effective agents for relieving pain and anxiety, morphine consumption by caged laboratory rats may be partly a response to laboratory conditions (Khantzian, 1974). The same possibility inheres in studies of self-administration through indwelling catheters. In these, rats are subject to the additional discomfort of catheterization and connection by a leash or linkage arm to an injection apparatus. An investigation of the degree of importance of housing conditions to morphine self-administration would clarify how far these studies should be generalized.

This study was designed to contrast oral morphine self-administration of isolated rats with that of rats in the least isolated and least confining conditions that could be contrived in the laboratory.

Materials and Methods

Subjects

The subjects were 32 albino rats of Wistar origin purchased from the University of British Columbia colony. They had continuous access to morphine solution and tap water for the three weeks immediately preceding the present experiment. During that period, they all consumed water almost exclusively. They were 103–107 days of age at the beginning of the experiment. Four females and 6 males comprised the isolated group at the outset; 10 females and 12 males comprised the social group.

Apparatus

Isolated rats were housed singly since weaning in 18 × 25 × 18 cm metal cages. The sheet metal sides prevented visual contact with adjacent animals. Rats received tap water and/or morphine hydrochloride solution (0.5 mg/ml) through stainless steel tubes from bottles fastened on the outside of the cages.

The rats in the social group lived together since weaning in an open-topped plywood box with 8.8 m^2 of floor area, a layer of sawdust on the floor, about a dozen, small open-topped cages that the rats could freely explore, and a 0.7 m climbing pole.

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Rats obtained fluid by entering a transparent plastic runway (inside measurements 4.7 cm × 5.8 cm × 24 cm) at the end of which were two liquid dispensers, one containing tap water and the other 0.5 mg/ml morphine hydrochloride in tap water. Each dispenser was positioned over a small well and a light beam. The rat broke the light beam while consuming the liquid, and when it withdrew its head the light beam was reconnected and another drop dispensed. The drop count for each dispenser was displayed on counters. When a rat entered the tube, it triggered a video camera, which recorded the display on the counters and the identifying mark on the back of the incoming animal.

Procedure

There were four experimental periods, labeled the Limited Access Period, the Forced Consumption Period, the Nichols Cycle Period, and the Abstinence Period.

Limited Access Period. The rats were placed on a schedule similar to that used by Stolerman and Kumar (1970), in which they were allowed access to fluids for approximately 7 h each day. The first day was a choice day, with both water and morphine hydrochloride solution available. The next 2 days the animals were given 7 h of access to morphine solution only. This 3-day cycle was repeated nine times, after which there was a final choice day.

Forced Consumption Period. The rats were given continuous access to morphine solution, and no water, for the next 57 days except for days 16, 38, 42, and 43, in which they were given a 24 h choice between morphine solution and water. During this period two females in the social group and two females in the isolated group died.

Nichols Cycle Period. The animals were then put on a 3-day schedule with access conditions changing every 24 h. No fluid was present on the first day, morphine solution only on the second, and water only on the third. The cycle was repeated eight times, with morphine-water choice days after the second, fourth, sixth, and eighth cycles. The schedule was adapted from one shown by Nichols et al. (1956) to increase morphine consumption in pre-addicted rats.

Abstinence Period. Morphine was then removed, although food and water remained freely available. The rats were given one 24-h choice day with access to water and morphine after 2 weeks and another after 5 weeks of abstinence. One female in the social group died before the final choice day.

Because of the deaths of five females, the final sample sizes for data analysis were: isolated females, 2; isolated males, 6; social females, 7; social males, 12.

The consumption of water and morphine solution by the rats in the isolated group was determined by weighing the bottles at the beginning and end of the choice days. The differences were corrected for spillage, which was determined by weighing two control bottles identically treated but kept on an empty cage. Spillage varied between 1–3 g/bottle/day. For the social group, consumption data were obtained from the drop recorder. Sides on which the two fluids were presented were changed irregularly for both groups.

Water consumption and morphine consumption as g morphine solution, as proportion of morphine solution to total fluid consumed, and as mg morphine HCl/kg body weight for each choice day were converted to square roots transforms to reduce heterogeneity of variance and were analysed with a least squares analysis of variance. Sums of squares were obtained using an experimental design analysis (Overall and Spiegel, 1969; Method 2).

Results

The direction of group differences for the three parameters of morphine consumption was identical and the pattern of statistical significance was very similar. The complete analysis for mg morphine HCl/kg body weight is presented here.

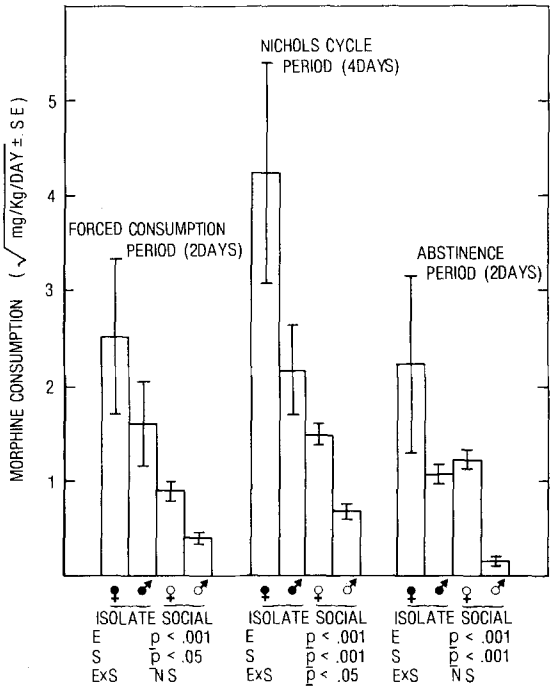

Fig. 1. Morphine consumption on choice days (mean square root transforms of mg morphine HCl/kg body weight/day ± SE) with significance levels from analysis of variance for each period (E = environment; S = sex)

Limited Access Period. Very little morphine was consumed by the rats of either group during choice days of the Limited Access Period and measurement reliability was not satisfactory for the social group. These data will not be presented here, although the trend is the same as the later data.

Forced Consumption Period. Daily forced consumption of morphine solution increased gradually throughout the Forced Consumption Period. Mean consumption, excluding the first 2 weeks during which consumption was considerably lower, was 26.6 g of morphine solution per day per rat for the isolated rats (13.3 mg morphine HCl/rat). The social rats consumed a mean of 37.2 g of morphine solution per day (18.6 mg morphine HCl/rat).

Morphine consumption was low on the early choice days during this period, but gradually increased. By the last 2 choice days, shown in Figure 1, an appreciable amount was consumed and there was a significant difference between groups. The isolated rats drank more solution than the social rats ($F = 21.46$, $df = 1/23$, $P < 0.001$), and the females drank more than the males ($F = 7.26$, $df = 1/23$, $P < 0.05$). The environment × sex interaction was not significant.