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BRIEF COMMUNICATION

# Saccharin Effects on Morphine-Induced Temperature Change in Rats

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BOWERS, R. L., L. D. NICASTLE AND D. C. FALB. *Saccharin effects on morphine induced temperature change in rats.* PHARMACOL BIOCHEM BEHAV 46(2) 483–485, 1993.—The effects of saccharin on morphine-induced temperature change was examined in Long-Evans rats. Rats were given free access to 0.15% saccharin for 15 days, followed by saccharin deprivation for 9 days. Saccharin was then returned to one group, while a second group received water. All rats were then injected with morphine sulfate (2 mg/kg), and postinjection temperatures were assessed over 75 min. The results showed that saccharin enhanced the biphasic effects of morphine by significantly increasing the hypothermic phase. The findings support the view that sweet substances influence endogenous opioid release.

Saccharin Morphine Temperature Endogenous opioids Rats

PAST research indicates that morphine produces biphasic effects on core body temperature. Following morphine injection, hypothermia occurs initially but is rapidly replaced by hyperthermia (1,3,5). The magnitude of the biphasic effect is modified by morphine dose. At low doses (i.e., 10 mg/kg or less), the hypothermic phase may be brief, or undetected, followed by a prolonged phase of hyperthermia; high doses of morphine (20 mg/kg or greater) produce longer periods of both hypothermia and hyperthermia (5,8,10).

Interestingly, gustatory processes, such as the ingestion of saccharin, appear to influence morphine effects on conditioned place learning, analgesia, and morphine self-administration (2,4,6,11). These findings provide indirect evidence that sweet-tasting substances may influence endogenous opioid release [cf. (7)]. More specifically, acute exposure to saccharin increases opioid release while chronic expose attenuates opioid levels (2,4). With this is mind, the purpose of the present study was to examine whether saccharin affects morphine-induced temperature change. If acute saccharin exposure indeed increases endogenous opioids [cf. (4)], we might expect that saccharin consumption may augment morphine temperature-related effects.

To test this notion, the saccharin-elation procedure (9) was employed to maximize saccharin consumption. More specifically, consumption of flavored liquids (e.g., saccharin, alcohol) increases dramatically when continuous access has been withdrawn for several days (9,10,13,14). In the present experiment, two groups of rats were exposed to saccharin for several days, followed by a period in which saccharin was removed. Prior to morphine injection, saccharin was returned for one group, and morphine-induced temperature change was assessed for both groups over a 75-min period.

If saccharin increases opioid release, animals exposed to saccharin should show a greater hypothermic response than animals that were not presented with saccharin. Rather, we might expect saccharin-exposed animals to respond as if they were given a larger dose than actually administered.

## METHOD

### *Subjects*

Ten female and male Long-Evans hooded rats, weighing 250–470 g, served. All rats had free access to rat chow (Teklad Rodent Diet) throughout the experiment. Animals were maintained on a 14 L : 10 D cycle with overhead fluorescent lighting.

### *Apparatus*

Individual Plexiglas chambers (internal dimensions: 47 × 37 × 20 cm) with stainless steel wire lids were used. Two graduated glass drinking tubes (Pyrex 100 ml) were inserted through holes in the center of each 37-cm end wall. The spouts

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were mounted 7 cm from the cage floor and protruded 3 cm into the chamber. Beta-Chips lined the floor of each cage. A Sensortek thermometer (Model BAT-12) with a Sensortek probe (Type T thermocouple) was used to assess all rectal temperatures.

*Procedure*

Ten rats were randomly assigned to the 9-S or 9-D group (described below). During the next 15 days, animals in both groups were given 24-h access to spouts containing tapwater or 0.15% saccharin. Milliliters of liquid consumed was recorded and fresh water and saccharin were provided daily. On day 16, saccharin was replaced with tapwater over the next 9 days.

On day 26, rats in the 9-S group were given access to saccharin for 20 min. Following saccharin exposure, core body temperature was assessed and then all rats received SC injections of morphine sulfate (2 mg/kg) and were returned to their cages. Postinjection temperatures were then recorded 15, 45, 60, and 75 min after injection. The 9-D group was treated identically to the 9-S group described above except saccharin was not returned prior to morphine injection; both spouts contained water.

## RESULTS

Figure 1 shows mean temperature change across the postinjection readings for the groups of rats exposed either to saccharin or water prior to morphine injection (i.e., 9-S and 9-D). Temperature change was determined by subtracting subjects' baseline temperature from each of the postinjection temperatures. Data points above the horizontal broken line indicate that postinjection temperature was above baseline measurement; data points below the line represent relative hypothermic effects.

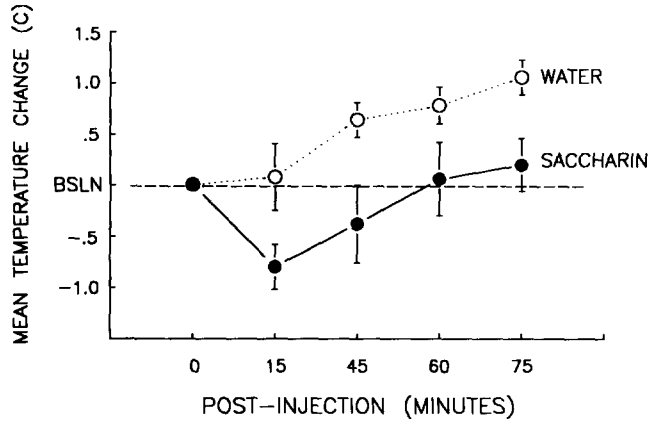


FIG. 1. Mean (± SEM) temperature change for animals exposed to saccharin or water prior to morphine injection.

As can be seen, rats that received exposure to saccharin showed consistently lower temperature change than rats that receiving water. A mixed analysis of variance (ANOVA) performed on the temperature data confirmed these results. The analysis revealed significant main effects for group, $F((1, 8) = 6.72, p < 0.03$, and time, $F((3, 24) = 13.35, p < 0.0001$. No group × time interaction was found, $F((3, 24) = 0.27, p > 0.05$. Finally, saccharin consumption was equivalent for the 9-S (mean = 66 ml; SEM = 14) and 9-D (mean = 66 ml; SEM = 23) groups prior to treatment.

## DISCUSSION

The present findings indicate that saccharin modifies both the hypo- and hyperthermic effects of low doses of morphine. These results support indirect but converging evidence that sweet-flavored substances such as saccharin modify endogenous opioid release [cf. (7)]. Although the effects of saccharin on morphine-induced place learning and morphine self-administration has been documented (6,11), no research has investigated whether saccharin plays a role in morphine temperature change. The findings suggest that saccharin effects are more general as they influence not only analgesia and reward but also core body temperature.

Perhaps the most surprising finding was the magnitude of the saccharin effect. The prolonged hypothermic phase observed in the saccharin group is consistent with extended hypothermia that typically occurs in animals given large doses of morphine (5,8,11). At this point, it is unclear whether the saccharin-elation procedure was responsible for the large effects shown. Perhaps future research may determine whether periodic withdrawal of saccharin or mere consumption is more important. Regardless, the findings clearly indicate that gustatory mechanisms may play a role in morphine control of temperature.

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