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# A Small Dose of Morphine Increases Intake of and Preference for Isotonic Saline Among Rats

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BERTINO, M , M L ABELSON, S H MARGLIN, R NEUMAN, C A BURKHARDT AND L D REID *A small dose of morphine increases intake of and preference for isotonic saline among rats* PHARMACOL BIOCHEM BEHAV **29**(3) 617–623, 1988 —Water-deprived rats were given hourly opportunities to ingest physiological saline and water for a number of days until they were taking substantial amounts of both solutions Prior to some opportunities to ingest, they were injected with either morphine (2 0 mg/kg) or a placebo Across a variety of procedures, morphine increased intake of and, in 1-hr tests, increased preference for 0 9% NaCl Intake of 1 5% NaCl also increased after administration of morphine These data suggest that endogenous opioids are involved in sodium intake These data also provide further support for the idea that one or more of the endogenous opioid systems are involved in the regulation of ingestion

Opioids Salt intake Salt preference Morphine Endogenous opioids

INTAKE of flavored solutions is influenced by the administration of opioid agonists and antagonists (see [16] for a review) This has been most extensively studied using rats and sweet tasting substances At low doses, morphine (MOR) increases intake of sucrose solutions [6], saccharin solutions [4,18], and sweetened alcoholic beverages [9] Relatedly, administration of either of the opioid antagonists, naloxone or naltrexone, reduces intake of solutions of sucrose [15], glucose [11], and saccharin [11] They also reduce preferences for solutions of saccharin [11] and of glucose [11] Results such as these have led to the hypothesis that the endogenous opioids are involved in mediation of pleasant aspects of the sweet taste [2,16]

For more than 50 years, there has been extensive research into rats' appetite and preference for salt [7,17] Considerable evidence suggests that at certain concentrations the taste of sodium chloride in water is pleasant to rats Rats of many strains prefer to drink hypotonic and isotonic saline to water, even when post-ingestional cues have been removed through the use of esophageal fistulas [13] Also, rats' facial expressions to the taste of salt contain some of the same components found after tasting sucrose [1] If the pleasantness of the taste of hypotonic and isotonic salt solutions is mediated in a way similar to sucrose and if opioids mediate sucrose's pleasantness, then opioid agonists and antagonists should influence intake of hypotonic and isotonic salt solutions in a manner similar to that of sucrose solutions

In apparent support of the above hypothesis, naloxone has been reported to decrease intake of solutions of isotonic saline [5] as it does for many kinds of ingesta [16] However, one cannot safely make inferences from only the observations of an antagonist's effects [16] One has considerably more confidence in an inference concerning the relevance of a particular neurochemical system (in this case, one or more of the endogenous opioid systems) to a particular class of behavior (in this case, ingestion), if an agonist (in this case, MOR) produces opposite effects to that of the antagonist (in this case, naloxone which reduces ingestion)

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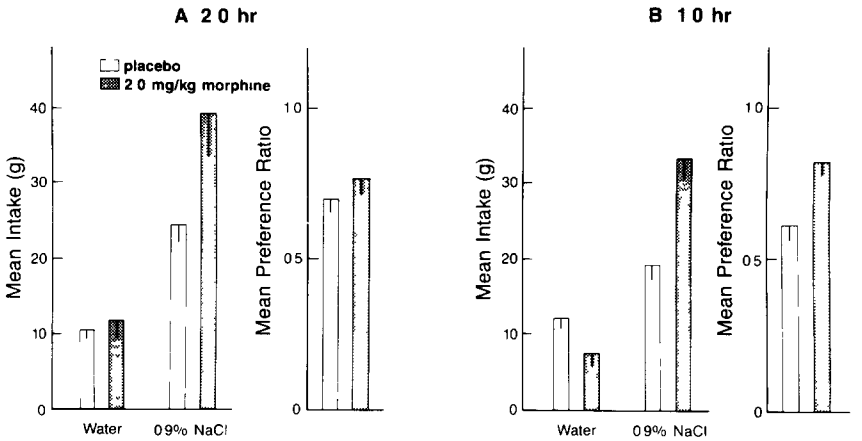


FIG 1 (A) The left graph depicts two-hr intake of salt water (0 9%) and water in 22-hr water-deprived rats (n=9) The right graph depicts the proportion of total fluid consumed as salt water (preference=g 0 9% NaCl consumed/g total fluid consumed) (B) The left graph depicts 1-hr intake of 0 9% NaCl and water in 23-hr water-deprived rats (n=9) The right graph depicts the proportion of total fluid consumed as salt water (preference=g 0 9% NaCl consumed/g total fluid consumed)

Administration of MOR with respect to saline intake has produced some conflicting results MOR has been reported to increase nighttime preferences for isotonic saline in rats while leaving daytime preferences unaffected [20] In mice, MOR has been reported to increase preferences for 3% NaCl but did not affect preferences for less concentrated solutions [10] Two preliminary attempts in our laboratories failed to demonstrate a reliable effect of small doses of MOR on salt water intake and preference In one preliminary attempt, water-replete rats were given a choice between water and isotonic saline for 1, 2, and 3 hr during the dark period of the light/dark cycle. MOR (2, 4 or 8 mg/kg IP) did not increase intake of or preference for isotonic saline Baseline intakes of these subjects, however, were low and there were only 5 rats in each group (Bertino, unpublished data) In another preliminary experiment [8], adult male rats were deprived of water for 4 hr and then at the beginning of their dark cycle, given one-hour, 2-bottle choices between water and one of four NaCl concentrations (0 09, 0.9, 2 85 or 9.0 % w/v) Naloxone (1.0 and 10 0 mg/kg) reduced intake of both water and the salt solutions. MOR, at doses incrementing intake of saccharin solutions (2 0 mg/kg), increased mean intake of the salt solutions but not reliably

Since small doses of MOR do lead to increased intake of sweet solutions, and in the preliminary experiments did not affect salt intake, it was tempting to speculate that MOR specifically affects intake of sweet substances or foods typically associated with high caloric density [16] Our failure to see a reliable increase in consumption of salt water with MOR, however, were based on small numbers of subjects or testing periods that were potentially too short Since it has been shown that the agonists and antagonists probably exert their facilitating and inhibiting effects at the end of a drinking session [6,18], it may be necessary to have testing sessions of long duration and to have an initially high level of baseline drinking to see a small-dose-MOR-effect, conditions not met in our preliminary studies Consequently, we decided to further study the effects of a small dose of MOR on rats' intake of isotonic saline

## EXPERIMENT 1

The first procedure of this experiment assessed the effects of a small dose of MOR on intake of water or physiological saline in rats deprived of water using 2-hr testing sessions, sessions sufficiently long to show an effect MOR increased intake of isotonic saline, so, we then instigated a second procedure, using the same rats and dose of MOR, but using a testing session of only 1 hr

### METHOD

*Subjects and Apparatus*

Nine male, experimentally naive, Sprague-Dawley rats (Taconic Farms) (mean weight=425 g) were housed individually in a colony room with constant temperature (24°C) and a 12/12 light-dark cycle (lights on at 0800) They were maintained on Wayne Rodent Blox ad lib and on a water-deprivation schedule as specified Fluids were presented in the home-cages by way of bottles with ballpoint sipping tubes Bottles were weighed to the nearest 0 1 g before and after presentation of fluids and corrected for spillage [14].

*Procedure*

Beginning 10 days before the first injections, rats had the opportunity to drink tap-water and 0 9% NaCl for only 2 hr/day beginning at 1200 Across the next 5 days, subcutaneous injections of either MOR sulfate (2 0 mg/kg) or placebo (0 9% saline, the carrier of MOR) were given 10 min before the drinking sessions There were two injection regimens Five rats received MOR on Days 2 and 4 while four received it on Days 3 and 5 During the remaining days, all rats received placebo All injections were 1 ml/kg

After the last day of the first procedure, the rats continued on the same daily drinking schedule except that the test session was reduced to 1 hr and, therefore, the period of deprivation was 23 hr After 9 days on the new schedule, exactly the same regimen of injections as used with the first procedure began

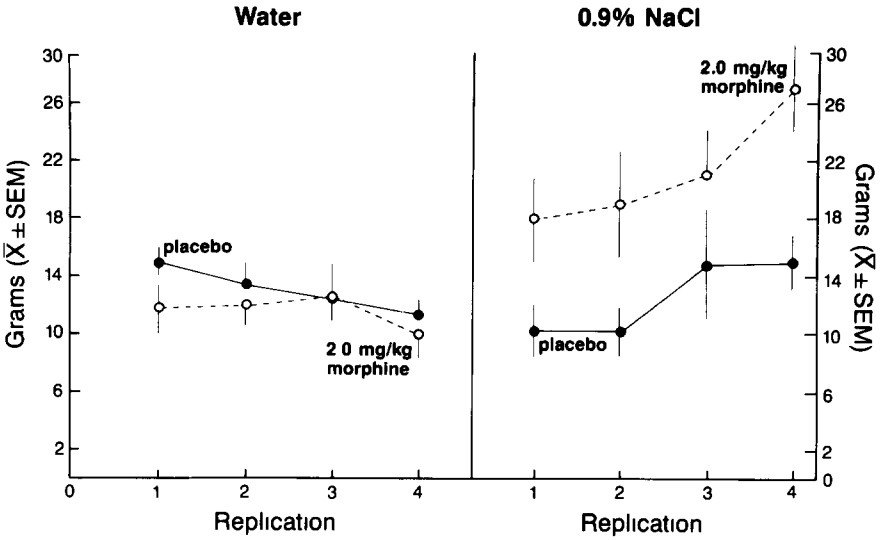


FIG 2 Intakes of water and 0 9% NaCl in 23-hr water-deprived (n=15) receiving four MOR and four placebo injections

With respect to each procedure, preliminary analyses indicated that there were no reliable differences among intakes under placebos Also, with respect to each procedure, preliminary analysis also indicated no reliable differences in intakes between the first and second administrations of MOR Additionally, similar results were achieved with those rats given MOR one day before their counterparts Consequently, the mean of the scores under MOR and the mean of scores under placebo (on the day before MOR injections) were used as a summary of a rat's intakes under placebo and MOR, respectively These data reductions yielded a single score for water intake and salt intake under placebo and drug for each rat and each procedure From these basic scores, preference ratios were calculated: g salt water ingested/total fluid ingested

## RESULTS AND DISCUSSION

Figure 1 summarizes the effects of MOR on intake of fluids MOR administration increased saline intake during the 2-hr test, $t(8)=3\ 33$, $p<0\ 02$ (Fig. 1A), as well as during the 1-hr test, $t(8)=7\ 2$, $p<0\ 001$ (Fig 1B) Water intake was not reliably modified during the 2-hr session by MOR, but was reliably reduced during the 1-hr session, $t(8)=-5\ 80$, $p<0.001$ Preference ratios did not change reliably when measured 2 hr after MOR administration When intakes were measured for only 1 hr, however, preference ratios for 0 9% NaCl were significantly increased with MOR from 0 61 (±0.050 SEM) to 0 82 (±0 036 SEM), $t(8)=7\ 52$, $p<0\ 01$

Clearly, MOR increased intake of isotonic saline. However, the question that should be addressed is why these results were not seen in the preliminary studies A more detailed analysis of the results from this experiment may give some indication of why the effects of MOR were not seen earlier

Under the 2-hr test, not all rats showed the effect Rats that did not initially drink the saline after placebo injections did not drink saline after injections of MOR One rat's saline intake decreased after MOR On the other hand, some rats' increment in saline intake were very large One rat that consumed large amounts of saline under placebo conditions (42 g) drank an excessive amount after MOR administration (98 g) Thus, in studies having a small n, the average effect may not emerge from individual differences

## EXPERIMENT 2

There are other procedural variables that may affect the likelihood of observing an increment in intake of isotonic saline after injections of MOR The rats in the 1-hr test, which showed a clearer effect than those of the 2-hr test, had prior experience with MOR (i.e , the 2-hr test), and this may have somehow primed the rats to allow the effect of MOR to emerge The effect of experience with MOR upon subsequent ingestion of saline was probed in this and the following experiment

## METHOD

Fifteen experimentally naive, male rats (mean weight=390 g) of the same strain and supplier as those of Experiment 1 began a daily regimen similar to that of Experiment 1. The injection regimen employed was the same as in Experiment 1 except it continued an additional 5 days so that all rats received a total of 4 placebo and 4 MOR injections. Rats were water-deprived for 23 hr and beginning at 1200 given 1 hr to ingest water and 0 9% saline. Intakes were analyzed with a three-way analysis of variance (ANOVA) (repeated measures) with injection type (MOR or placebo), replication (1, 2, 3, or 4), and fluid type (0.9% NaCl or water) as factors

## RESULTS AND DISCUSSION

As rats continued the daily regimen, their water intake decreased and their salt solution intake increased (Fig. 2) Regardless, however, MOR both increased salt solution intake, $F(3,42)=4.22$, $p<0\ 01$ and decreased water intake, $F(1,14)=4\ 90$, $p<0\ 04$, across tests Thus, prior experience

of ingesting salt solutions after MOR is not necessary to observe a MOR-induced increment in intake of 0 9% NaCl during a 1-hr test Although the interaction of replications and injection types was not significant, one might make the case that the likelihood of observing a MOR effect during testing is enhanced after rats are clearly taking considerable test solution

Overall preference scores were obtained by averaging salt solution and water intakes over the 4 days and then calculating the salt preferences from these averages The salt preference score averaged 0 47 (±0 051 SEM) in the placebo condition and 0 62 (±0 054 SEM) after MOR, $t(14)=3\ 91$, $p<0\ 01$

## EXPERIMENT 3

Although the results of Experiment 2 do not confirm the hypothesis experience with MOR is a necessary condition in order to observe MOR's facilitation of salt intake, MOR's initial effect may still have distracting, frightening or aversive elements which wane with repeated administrations In this experiment, therefore, MOR was administered 13 days before the rats were fluid-deprived and tested for isotonic saline intake Consequently, MOR's effects would not be novel for some subjects during the testing

### METHOD

*Subjects*

Forty-eight male, Sprague-Dawley rats (Taconic Farms) were housed as the animals in Experiment 1 and had Wayne Rodent Blox available ad lib throughout this experiment From their arrival at the laboratory until the beginning of this experiment they were handled nearly every day When they reached 245–362 g, they received either MOR (2 0 mg/kg) or placebo (0 9% saline) injections across a 6-day period

One group of rats (n=16) received only placebo injections (0 MOR experiences), one group (n=16) received MOR every other day with placebo on alternate days (3 MOR experiences), and one group (n=16) received daily MOR injections (6 MOR experiences) Thirteen days after the last injection, rats were placed on the 23-hr water-deprivation and testing schedule

*Procedure*

Rats were presented with water and 0 9% NaCl available for 1 hr/day at 1300 Injections began 7 days later All subjects received placebos on Day 1 On Day 2, half of the rats in each prior experience group received MOR whereas the remaining half received a second placebo On Day 3, the rats were reversed from Day 2 in regards to whether they received a MOR or placebo Half of the animals in each prior experience group received their drinking fluids immediately after the injections whereas the other half received fluids 15 min after the injections

The experimental design conforms to a 3×2×2×2 factorial ANOVA for repeated measures, with factors of MOR experience (0, 3, or 6 experiences), the two injection schedules (schedule A placebo, placebo, MOR, or schedule B placebo, MOR, placebo), the time after injection that drinking fluids were given (immediately or with a 15-min delay), and type of injection (MOR or placebo) Intakes of salt solution, water and preference ratios were analyzed with separate ANOVAs

### RESULTS AND DISCUSSION

MOR increased intake of saline, $F(1,36)=16\ 56$, $p<0\ 0002$, and decreased water intake, $F(1,36)=16\ 49$, $p<0\ 0003$ There was a significant drug × schedule interaction, $F(1,36)=5\ 46$, $p<0\ 02$, on saline intake Rats on the A schedule (placebo, MOR, placebo) had greater increases in saline intake after MOR injection than rats on the B schedule (placebo, placebo, morphine) The only other significant effect was a schedule × time after injection interaction, $F(1,36)=6\ 17$, $p<0\ 02$ Here the 15-min delay condition increased water intake in the A group whereas it slightly decreased water intake in the B group Preference ratios averaged 0 38 after placebo and 0 51 after the MOR, $F(1,36)=11\ 97$, $p<0\ 002$ Differential experience with 0 to 6 injections of MOR and test delays up to 15 min after injections had little influence on the propensity to increase intake of salt solutions after a small dose of MOR

In this experiment and in Experiment 2, preference ratios were clearly enhanced by small doses of MOR In the 2-hr test of Experiment 1, preference ratios were not increased by MOR even though intakes of salt water were reliably increased We presume that the extended opportunity to drink water provided in the 2-hr test and the resulting increase in water intake (which diminished the difference in preference ratios) could reflect a compensatory balancing of electrolytes

## EXPERIMENT 4

In all the previous experiments, 0 9% NaCl was the solution available with water Generally, non-water-deprived rats drink more isotonic saline than water Here we assess the effects of a small dose of MOR on intake of 1 5% NaCl, a generally non-preferred solution

### METHOD

Eighteen male, experimentally naive rats of the same strain as in Experiments 1–3 served as subjects Rats were water-deprived for 22 5 hr and beginning at 1200 hr they were given water and 1 5% NaCl to drink This schedule continued for 8 days whereupon rats were started on a regimen of injections identical to that of Experiment 1 except that MOR was given 5 min before their drinking period Intakes were analyzed with a three-way ANOVA with three repeated measures having factors of fluid type (salt solution or water), replication (first and second measure), and injection type (MOR or placebo) Preference ratios were also analyzed with a two-way ANOVA with two repeated measures factors, i e , with factors of replication and injection type

### RESULTS AND DISCUSSION

The main effect of fluid type was statistically significant with rats drinking more water than salt solution, $F(1,17)=47\ 46$, $p<0.001$ The main effect of injection type (MOR vs placebo) was also statistically significant with rats drinking more fluids after the injections of MOR, $F(1,17)=22\ 70$, $p<0\ 001$ The replication × injection type interaction was statistically significant, $F(1,17)=8\ 82$, $p<0\ 01$ Inspection of Fig 3 shows that this was due to a greater increase in fluid intake following the second injection of MOR Finally, the three-way interaction was statistically significant, $F(1,17)=5\ 00$, $p<0\ 05$ Post-hoc comparisons demonstrated that after the second MOR injection, intakes

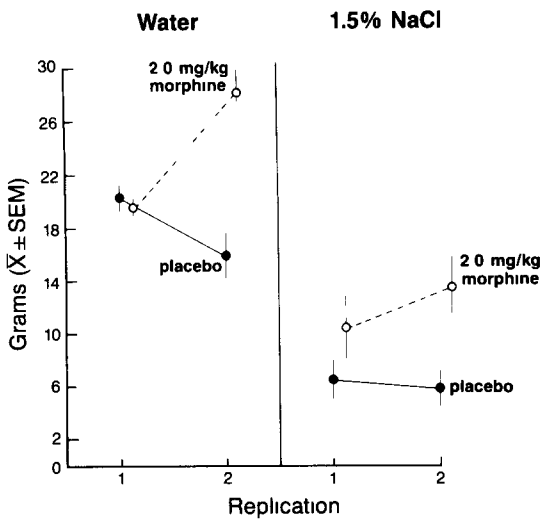


FIG 3 Intake of water and 1 5% NaCl in 22 5-hr water-deprived rats (n=18) after two MOR and two placebo injections

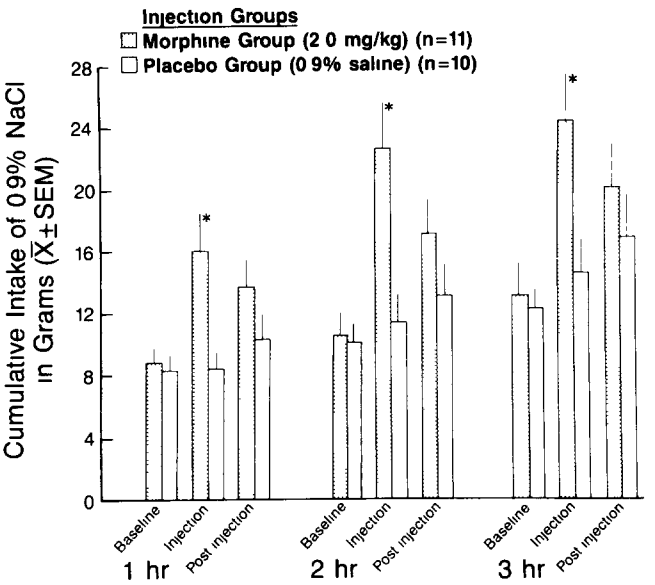


FIG 4 Intake of 0 9% NaCl in 21-hr water-deprived rats after repeated MOR (n=11) or placebo (n=10) injections

of salt solutions and were reliably greater than intakes after the placebo ($p<0$ 05, Bonferroni $t$) Overall, preference ratios tended to be greater after the MOR injections, although this did not reach acceptable levels of statistical significance, $F(1,17)=4.17$, $p<0$ 06 Thus, MOR induces rats to drink more hypertonic salt solution as it does isotonic saline

## EXPERIMENT 5

In this experiment, we increased the number of MOR injections to further test whether the MOR-induced increase in salt intake would endure beyond administration of MOR There was also an interest in seeing whether or not the small-dose-MOR-effect would wane with repeated injections. The preceding four experiments were conducted at Rensselaer Polytechnic Institute The following experiment was conducted at the Monell Chemical Senses Center

### METHOD

Twenty-one male, Sprague-Dawley rats (supplied by Charles River) were housed singly in stainless steel cages (21×36×17 cm) in a temperature and humidity controlled room (22°C) The 12/12 light cycle was advanced such that the lights were extinguished at 1430 The rats were maintained on Purina Rodent Chow 5001 ad lib They were kept on a 21-hr water deprivation cycle where bottles were removed at 1300 Beginning at 1000, two graduated centrifuge tubes were attached to the front of the cages, one containing tap-water and the other containing a 0 9% NaCl solution The bottles remained on the cages for 3 hr Readings of baseline intake to the nearest 0 5 ml were taken each hour for 7 consecutive days (Days 1–7) One-hour intakes of water and 0 9% NaCl were averaged across the 7 days and two groups of rats were formed, matched on these 1-hr 0.9% NaCl intakes Beginning with Day 8 and continuing for 7 days (through Day 14), one group of rats (n=11) received subcutaneous injections of MOR sulfate (2 0 mg/kg) while the other group (n=10) received an equivolume injection of isotonic saline Seven days of post-injection intakes were recorded (Days 15–21).

To test for the stability of effects across the 7 days of injections and post-injections, separate ANOVAs were computed on the scores of salt intake for each hourly reading with days as a repeated measure factor At 1 and 2 hr, there was no reliable interaction of days and treatment group (see the Results section) Thus, cumulative intakes of water and 0 9% NaCl at 1, 2 and 3 hr were averaged across the 7 days of each period. These were analyzed separately at 1, 2 and 3 hr with a three-way analysis of variance with one between subjects factor (injection group MOR or placebo), and two within subjects factors (period baseline, injection period, post-injection, fluid type· water or 0 9% NaCl) Preference ratios (g 0 9% NaCl ingested/g total fluid consumed) were also computed on the 7-day mean intakes of each period These were analyzed separately for each hour with a two-way analysis of variance with injection group and period as factors In all analyses, when interactions were significant, post-hoc comparisons were made using the Bonferroni $t$-test

### RESULTS

*One-Hour Intakes*

MOR administration increased intake of 0 9% NaCl but not water during the first hour of measurements (Fig 4), as shown in the three-way interaction, $F(2,38)=5$ 52, $p<0$ 01 Post-hoc tests showed that during MOR injections, rats drank more 0 9% NaCl than placebo rats ($p<0$ 05) There were no group differences in baseline and post-injection salt solution intakes

Overall, the MOR-injected group drank more 0.9% NaCl than water whereas the placebo group drank relatively more water, for the injection group × fluid type interaction, $F(1,19)=4$ 46, $p<0.05$ Total fluid intake increased across the periods, $F(2,38)=15$ 87, $p<0$ 001 Water intake in the MOR-injected group, and water and 0 9% NaCl intakes in the placebo rats remained relatively constant across the three periods (see Fig 5)

Relative to the placebo group, salt preference scores were elevated after rats received MOR injections, as shown by the

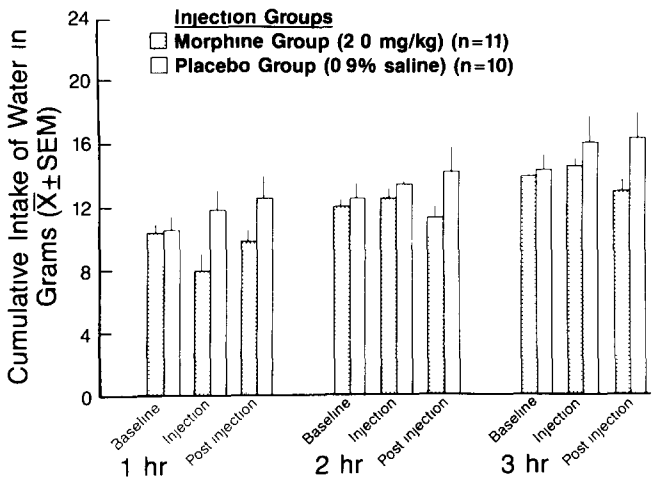


FIG 5 Intake of water in 21-hr water-deprived rats after repeated MOR (n=11) or placebo (n=10) injections

period × injection group interaction, $F(2,38)=4\ 42$, $p<0\ 05$, post-hoc, $p<0.05$ Preference scores in the MOR group increased from an average of 0 45 during the baseline period to 0 64 after MOR administration and decreased to 0 56 during the post-injection period Respective salt preference scores remained relatively constant in the placebo-injected rats and were 0 45, 0.42 and 0 44 Group differences in post-injection salt preference scores were not statistically significant

*Two-Hour Intakes*

The injection group × days interaction in analyses for the injection period and for the post-injection period were not statistically significant After averaging the days' data within each injection period, the three-way interaction was still significant, $F(2,38)=4\ 27$, $p<0\ 05$ Again, MOR-injected rats increased their intake of 0 9% NaCl over the placebo controls ($p<0\ 05$) There were no significant group differences in intake of salt solution during the baseline and post-injection periods

Water intake was unaffected by MOR administration Preference ratios increased from the first to subsequent periods, $F(2,38)=4\ 33$, $p<0\ 05$ Although the three-way interaction was not a reliable source of variance, salt preference scores in the MOR group increased during the injections (from 0 45 to 0 63) and decreased slightly (to 0 58) during the post-injection period. Respective scores for the placebo group were 0 44, 0 45 and 0 47

*Three-Hour Intakes*

Changes in salt intake across individual days in the injection and post-injection periods were first examined There was a statistically significant interaction of injection group and days during the post-injection period, $F(6,114)=4.27$, $p<0\ 01$ This was due to a decrease in salt intake during the first post-injection day in the MOR group The interaction disappeared when this day was removed from the analysis

When the days were averaged in each period and were analyzed, the three-way interaction was no longer significant Total fluid intake was greatest during MOR injections whereas for the placebo controls, fluid intake was greatest during the post-injection period, as shown by the period × injection group interaction, $F(2,38)=14\ 21$, $p<0\ 001$ Intake of salt solution after MOR was elevated relative to that of placebo controls ($p<0\ 05$)

Preference ratios were not reliably modified as a result of MOR, i e , the three-way interaction was not a reliable source of variance However, as in the 2-hr intakes, preference ratios tended to increase during MOR injections (from 0 47 to 0 61) and remained high during the post-injection period (0 61) Preference ratios of the placebo controls showed a slight increase across periods (0 46, 0 47 and 0 49, respectively)

## DISCUSSION

This last study confirms the four preceding it in that MOR increased intake of and preference for salt solutions in the 1st hr of testing Although intake of salt solution remained elevated at 2 and 3 hr after the MOR injection, salt preference ratios were not Examination of Fig 4 shows that the MOR-injected group's intake of salt solution was elevated relative to their baseline both during the injection and post-injection periods However, the differences between MOR and placebo groups were not significant in this post-injection period, since there was a trend for intake of salt solution to increase in the placebo group across the three periods

It could be argued that we may have missed a post-injection elevation in salt intake in the MOR group, because they were experiencing mild withdrawal on the 1st day after injections ended and this lowered the average post-injection score Salt intakes were lower on that 1st post-injection day in the MOR group However, when that day was removed from the averages, there was still no difference between groups in salt intake If there were a carry-over effect of MOR, it was not great The fact that during the injections, MOR increased only salt intake and not water intake, leads to the suggestion that MOR exerts its greatest effects on fluids containing distinctive tastes

## GENERAL DISCUSSION

Even though our preliminary studies mentioned in the Introduction did not provide evidence for concluding that small doses of MOR increment intake of salt water, it is now clear that a small dose of MOR can increment such intake Across five experiments and a variety of procedural variables including tests in two different laboratories, it has been shown that 2 0 mg/kg of MOR increments intakes of salt water much as MOR increments intake of other kinds of ingesta The hypothesis that a small dose of MOR only increments intakes of sweets or ingesta having high caloric significance [16] is not supported

This increased intake is consistent with the data documenting increased preference for sweet solutions and for high fat diets after MOR administration, all believed to be palatable Our results may suggest, as has been proposed for sweets [2], that endogenous opioids are involved in mediating pleasant aspects of the taste of salt The fact that MOR increased intake of both isotonic and hypertonic NaCl suggests that a substance need not be preferred in order to see this effect

In the preliminary studies mentioned in the Introduction, periods of deprivation were short-term or nil, resulting in low levels of intake MOR probably does not instigate ingestion, but more likely, prolongs ingestion once begun [6] It follows, therefore, that the effects of 2 0 mg/kg MOR only

emerge when there is already a substantial propensity to ingest. So, we *cannot* conclude that MOR under many or all circumstances will increase salt intake We can conclude with confidence, however, that a small dose of MOR can increase intake of salt water across a number of different procedural variables

Unlike the results from Experiments 1–3, repeated testing influenced outcomes in Experiment 4. Also, when session length was 2 or 3 hr (Experiments 1 and 5) rather than 1 hr, preference ratios tended not to increase due to the rats taking more water during the prolonged session We conclude, therefore, that the taking of salt interacted with the propensity to take water, and led, especially in the procedures of Experiment 4, to more water intake with experience of thirst due to the MOR-induced initial focus on salt intake

The inference from these observations and others, including observations of the effects of naloxone [19], is that a function of one or more of the endogenous opioid systems is the prolongment of ingestion once begun Prolongment of ingestion is, of course, adaptive when there is periodic scarcity of nutrients, a probable condition in much of our evolutionary history [3]. The mechanism of this prolongment could be an enhancement of the pleasant aspects of a taste [2,16]

An endorphinergic surfeit in the brain would, it seems, increase intake of sweets [2,16], salt (these experiments), fatty foods [12] and alcoholic beverages [9] The fact that we see no evidence for a diminution of effects with repeated administrations of MOR is supportive of the idea of an endorphinergic surfeit being a setting condition for increased consumption. The effect of repeated MOR administrations on salt intake is to be contrasted with the development of tolerance to analgesia after repeated MOR injections This difference suggests some divergence in the mechanisms by which MOR increases consumption and produces analgesia However, this lack of tolerance in MOR's effects on ingestion would be expected if endogenous opioids are involved in feeding

Our hypothesis is that MOR increases the pleasant aspects of the salty taste but, at this point, we do not know how MOR has peripheral (e g , morphine may induce transient hypotension) and central effects, many of which could be involved in increasing salt intake In future work, we plan to examine the relative importance of MOR's peripheral and central actions in increasing salt intake

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