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BRIEF COMMUNICATION

Morphine Suppresses Alcohol Drinking Regardless of Prior Alcohol Access Duration

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SINCLAIR, J. D. *Morphine suppresses alcohol drinking regardless of prior alcohol access duration.* PHARMAC. BIOCHEM. BEHAV. 2(3) 409–412, 1974. – Two groups of 14 male Sprague-Dawley rats were given either 1 or 32 days of voluntary access respectively to 7% (v/v) ethanol solution before being injected once with 30 mg/kg of morphine. Alcohol consumption during the subsequent week was suppressed to about the same extent in both cases. Food intake was slightly reduced and water drinking increased in both groups after the morphine injection. The only difference observed between the effects after 1 and 32 days of alcohol access was that in the latter there was a significant negative correlation ($r = -.891$) between the reductions in alcohol and food consumption. The results suggest that the suppression of alcohol drinking is not dependent upon those factors, such as the ability to show an alcohol-deprivation effect, which develop during prolonged access to alcohol.

Voluntary alcohol drinking Morphine Alcohol-deprivation effect Acquired alcohol tolerance
Water drinking Eating Morphine-induced weight losses

VOLUNTARY alcohol consumption has previously been found to be strongly suppressed for about a week after a single morphine injection in rats having at least 5 weeks of prior access to alcohol [4]. Concomitant intake of water and a saccharin solution was not reduced, while eating was depressed to a lesser degree and for a shorter period than alcohol drinking. Morphine given during periods when alcohol was not available eliminated the temporary increase in alcohol consumption, or "alcohol-deprivation effect (ADE)", usually observed when access is first returned [5,6].

There were several hypotheses which seemed capable of accounting for the suppressive effect of morphine on alcohol drinking. Of these, several of the more plausible explanations were dependent upon factors which develop only during prolonged access to alcohol. These hypotheses would, therefore, predict that little or no suppression should be found in relatively naive rats. This prediction was tested in the present study by administering morphine to 2 groups of rats, one with 32 days and the other with only 1 day of prior access to alcohol.

METHOD

Twenty-eight male Sprague-Dawley rats were given ad lib access to 7% (v/v) alcohol solution, prepared from 96% ethanol, plus tap water and the standard Alko rat food. After one day, they were divided into 2 groups matched on the basis of their ratio of ethanol to total fluid consumption, E/T. Group MS was then injected i.p. with 30 mg/kg morphine as the hydrochloride in a saline base, while Group SM was injected at this time with a similar volume of saline. Thirty-one days later the treatments were reversed: Group MS was given a single saline injection and Group SM a single 30 mg/kg morphine injection. All animals had continual voluntary access to alcohol solution throughout the experiment, i.e., 63 days. Subsequently, 7 of the rats, 3 from Group MS and 4 from SM, had their alcohol bottles removed and 15 days later were given a 30 mg/kg morphine injection.

All animals were individually housed in standard galvanized wire mesh cages. The rats and their food were weighed daily for the first week after each injection, and every second day throughout the remainder of the study. Because changes in alcohol consumption were being studied rather than the absolute level of it, the positions of the alcohol and water bottles were kept constant at all times.

RESULTS

Effect of Morphine on Alcohol Drinking

As shown in Fig. 1, there was a strong suppression of

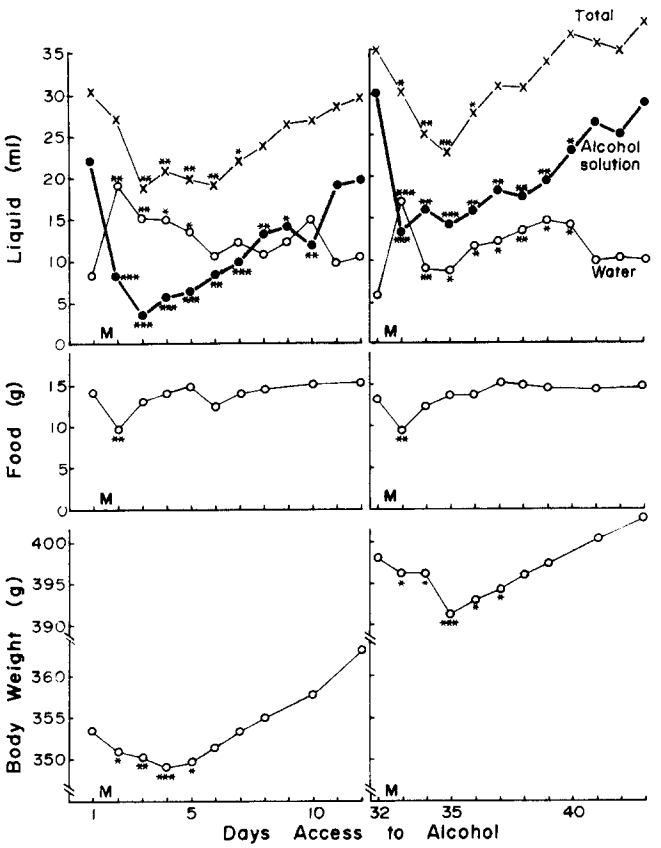

FIG. 1. The effect of a single morphine injection, at M, on subsequent alcohol solution, water, total fluid and food consumption and on body weight, in rats having either 1 day (on the left) or 32 days (on the right) of access to alcohol prior to the injection. Significant changes from the values obtained on the day before the morphine injection are indicated by $*p<0.05$, $**p<0.01$ and $***p<0.001$.

alcohol consumption after morphine administration, regardless of whether the injection was given after 1 or 32 days of alcohol drinking. Comparing the ml of alcohol/kg consumed after each morphine injection with the amount drunk on the day before the injection, there was a significant reduction in the first half of the experiment on each of the first 9 days, while in the second half the reduction was significant for each of the first 8 days. There was no significant difference between the total amount of alcohol-intake suppression shown after the 2 morphine injections, regardless of whether suppression was measured relative to their own pre-injection alcohol intake ($t = -0.56$, 26 *df*, $p>0.10$) or relative to the alcohol drinking by the control groups injected with saline ($t = 1.63$, 26 *df*, $p>0.10$).

Water Drinking, Food Intake, and Weight Loss

The mean changes in these variables were similar after each morphine injection (Fig. 1). Food intake was significantly reduced in both cases but only on the first day after morphine administration, and the percent reduction was not as great as it was for alcohol consumption. There was also a significant weight loss of about the same magnitude in both cases, reaching a maximum 3 days after morphine

TABLE 1

CORRELATIONS COEFFICIENTS (r) BETWEEN THE ABSOLUTE AMOUNTS OF CHANGE IN DIFFERENT VARIABLES AFTER A 30 mg/kg MORPHINE INJECTION IN RATS WITH 1 (A) AND 32 (B) DAYS OF PRIOR ACCESS TO ALCOHOL

	Water Intake	Food Intake	Body Weight
(A)			
Alcohol intake	−0.596*	−0.038	+0.200
Water intake		+0.039	+0.198
Food intake			+0.601*
(B)			
Alcohol intake	−0.692†	−0.891†	−0.672†
Water intake		+0.451	+0.377
Food intake			+0.802†

$*p<0.05$ $\quad$ $†p<0.01$

administration. The control groups were gaining at rates of 1.4 and 1.5 g/rat/day after their saline injections on Days 1 and 32 respectively. Water intake increased significantly after both morphine injections, but not enough to compensate for the reduction in alcohol solution consumption, as shown by the decline in total fluid intake.

Correlations Between Variables

After the morphine injection on Day 1, there was nearly zero correlation between the amount of alcohol suppression and the reduction in food intake, and since a reduction in the drinking of alcohol solution (at 0.39 Cal/ml) resulted in a decrease in caloric intake, there was a slight positive correlation between the suppression of alcohol drinking and weight loss. After the morphine injection on Day 32, however, suppression of alcohol intake was very strongly negatively correlated with reduction in food intake and weight loss (see Table 1): i.e., the more morphine caused alcohol intake to be suppressed, the less reduction it caused in eating. Since the caloric content of food is greater (at 3.69 Cal/g), reducing alcohol intake and not food consumption kept the caloric intake higher and prevented large weight losses. At the other extreme are 2 rats which did not reduce alcohol drinking, in one case because no alcohol was being drunk before morphine was administered. These rats lost 26 and 15 g, in comparison to an average loss by the other 12 rats of only 4.8 g.

Effects of Morphine when Alcohol was not Available

When access to alcohol was eliminated for the 7 rats, they increased their food consumption from 13.63 g to 18.71 g, and their water intake from 8.77 ml to 30.09 ml by the end of 15 days. Subsequently, on the first 3 days after the morphine injection, their food intake decreased by an average of 7.5 g/rat/day, they lost an average of 15.6 g of body weight, and their water consumption was 30.14,

20.14 and 16.29 ml on the 3 days respectively. Consumption of food and water then returned to approximately normal on the fourth and subsequent days. The reductions in food consumption, body weight and water drinking were all significantly different from those shown by the 12 rats that had lowered alcohol intake after the morphine injection on day 32 ($t = 3.10$, 17 *df*, $p<0.01$; $t = 3.97$, 17 *df*, $p<0.001$; $t = 5.43$, 17 *df*, $p<0.001$).

DISCUSSION

The morphine injection given after 1 day of previous access to alcohol suppressed alcohol drinking as much as the morphine injection given after 32 days of access. The average effects of morphine on water intake, food consumption and body weight were also approximately the same in both cases. The only difference caused by prolonged prior access to alcohol was the production of a strong negative correlation between the reductions in alcohol and food consumptions.

It is possible that morphine caused alcohol intake to be suppressed by different means in the rats with only 1 day of alcohol access previously than in those with 32 days. However, because of the similarities between the effects in both cases, it seems more parsimonious to assume that morphine acted in the same way both times. If this is true, it can be concluded that the suppression was not dependent upon any factors which developed in the rats between 1 and 32 days of access to alcohol.

It has been previously shown that during this period rats develop the ability to show an alcohol-deprivation effect (ADE) [5]. They also often increase their daily alcohol intake during this time [6], as the controls here did, perhaps as a result of an acquired tolerance to alcohol. It had been felt prior to the present studies that these two factors were prime candidates for explaining the morphine-induced suppression of alcohol drinking. Interactions with the ADE were suspected because of the similarity between the time course for recovery from suppression, and the growth of the ADE as a function of how long alcohol was withheld [6], and because morphine given during periods when alcohol was not available eliminated the ADE [4]. Another possibility was that morphine may have reduced the factors responsible for the increase in alcohol consumption or acclimation during the initial weeks of access, thus returning alcohol intake to the pre-acclimation level. However, since rats with only one day of prior access to alcohol do not show the ADE [5] and have not yet acclimated to alcohol [6], these factors could not have been involved in the morphine-induced suppression which was observed here after only one day of alcohol drinking.

Similarly, the possibility that Nichols' general theory of addiction [2] explains the suppression is also lessened by this finding. According to this theory, rats learn to associate alcohol drinking with its ability to reduce basic drives such as hunger, fear, anxiety and sexual urges, and, consequently, these drives come to motivate alcohol consumption. Since morphine is thought to reduce many of these same drives, it could decrease the motivation to drink alcohol. However, unless all of the process of learning the drive-reducing properties of alcohol is completed during the first day of access, Nichols' theory could not account for the fact that the suppression was as strong after one day as it was after 32 days of alcohol drinking.

The results from the experiment in which morphine was given to rats without access to alcohol eliminate another possibility: i.e., that the decrease in alcohol drinking was a compensatory secondary result of increased water intake. Since rats without alcohol decreased their water drinking, it appears that the alcohol intake suppression was the primary effect and the increase in water drinking seen in rats having access to alcohol when morphine was given was a compensatory result.

The strong negative correlation between reductions in alcohol and food intakes found after the morphine injection on Day 32 but not after the injection on Day 1 remains somewhat puzzling. The correlation is consistent with the results obtained in the study in which rats did not have access to alcohol. These rats, which did not have alcohol to reject, and those after the injection on Day 32 which chose not to reduce their alcohol drinking, all showed a mcuh larger decrease in food consumption and because of the food's greater caloric content, a much larger weight loss. What is puzzling is the lack of such a correlation in the rats with only one day of prior alcohol drinking. As a group they responded like the animals with 32 days of alcohol access: their alcohol intake decreased about the same amount, which apparently kept them from reducing food consumption and losing weight to the degree that the rats without alcohol access did. But as individuals, this trade-off between alcohol and food reduction was not seen.

It has recently been reported that human narcotic addicts before turning to heroin drank substantially larger amounts of alcohol and had more problems with it than did a control population [1]. During the period when they used heroin, however, their alcohol intake was reduced approximately 51%, to about the level of the controls. In another recent study [3] with narcotic addicts it was found that "92 of the (100) patients said that alcohol use was decreased or eliminated when drug use was initiated", and when narcotics were used daily, 68 of them reported complete abstinence from alcohol and 30 of the remaining 32 reported a marked decrease in alcohol use. These results suggest the possibility that morphine or heroin may suppress alcohol drinking in humans as well as in rats, and increase the importance of finding the means by which morphine causes the suppression. The present studies show that it is not dependent upon having had prolonged previous access to alcohol, and thus narrow the field of possible explanations.

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