*Pharmacology Biochemistry & Behavior*, Vol. 37, pp. 633–638. © Pergamon Press plc, 1990. Printed in the U.S.A. 0091-3057/90 $3.00 + .00

# Methylenedioxymethamphetamine's Capacity to Establish Place Preferences and Modify Intake of an Alcoholic Beverage

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Received 27 February 1990

BILSKY, E. J., Y. HUI, C. L. HUBBELL AND L. D. REID. *Methylenedioxymethamphetamine's capacity to establish place preferences and modify intake of an alcoholic beverage.* PHARMACOL BIOCHEM BEHAV **37**(4) 633–638, 1990.—Doses of 0.2, 2.0, 6.3 and 20.0 mg/kg 3,4-methylenedioxymethamphetamine (MDMA), a putative neurotoxin at serotonergic neurons and a recreational drug, were assessed using Sprague-Dawley rats in the conditioned place preference (CPP) test. Also, the drug's effects on intake of a sweetened ethanol solution (ES) was assessed. The CPP testing involved multiple administrations of MDMA with frequent periodic testing (weekly for 4 weeks) of MDMA's effects. Doses of 2.0 and 6.3 mg/kg produced positive CPPs with every test. MDMA also affected rats' gain in body weight across the 4 weeks of dosing. The 2.0 mg/kg dose reliably incremented gain in body weight, while the 20.0 mg/kg dose reliably attenuated it. In the drinking experiment, water-deprived rats (22 h/day) were given daily opportunities to drink either tap water or a sweetened ES. When stable intakes were achieved, MDMA's effects were assessed across repeated daily administrations (12 days) and subsequently (16 days). MDMA, dose-relatedly, decreased intake of both ES and water with the highest dose leading to marked loss in body weight. Intakes of fluids were not modified markedly subsequent to dosing. In summary, MDMA is an agent that produces a positive CPP (providing further evidence for MDMA's abuse liability), produces changes in weight gain and nonselectively reduces fluid intake among fluid-deprived rats.

MDMA Methylenedioxymethamphetamine Positive affect Conditioned place preference Ethanol intake Drugs of abuse

FROM a number of perspectives, 3,4-methylenedioxymethamphetamine (MDMA), commonly referred to as "ecstasy," is an interesting drug. People have reported that MDMA produces pleasant feelings (1) and, consequently, it has become a drug of abuse. This is mirrored by the finding that MDMA is self-administered by laboratory subjects (12). There is also evidence leading to the conclusion that MDMA is toxic to serotonergic neurons [for a review, see (17)]. A loss of central serotonergic activity could lead to increases in intake of alcoholic beverages, since perturbations of serotonergic systems have been shown to affect rats' intakes of alcoholic beverages (6, 8, 16, 20, 23). With these ideas as background, the effects of MDMA were examined under two circumstances: (a) as an agent in a test for conditioned place preferences (CPPs) and (b) as an agent that might modify intake of a sweetened alcoholic beverage.

## EXPERIMENT 1

MDMA has been previously shown to lower the threshold for brain-stimulation reward among rats, an index of the potential euphoric properties of a drug. It does so, however, across a rather restricted range of doses (approximately 1 to 4 mg/kg) (10). This may be due to MDMA's debilitating effects that could be produced by larger does. The procedures of CPP testing assess an agent's effects, after conditioning, while the rats are undrugged. Therefore, CPP testing is useful for assessing the affective states produced by doses of drugs which produce debilitating effects (2). Consequently, in this experiment, we tested the effects of a range of doses of MDMA using the CPP test.

It has been reported that MDMA is toxic to serotonergic systems even after only a single subcutaneous (SC) administration of 20 mg/kg (15). Given such toxicity, it is possible that MDMA's effects might change rapidly across repeated administrations. The CPP test allows for repeated conditioning and testing of an agent's effects, and thus an assessment can be made of an agent's ability to sustain a CPP. Continued conditioning with morphine, for example, sustains or even enhances a CPP (14). Consequently, the

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putative effects of MDMA-induced neurotoxicity were assessed with respect to its ability to sustain a CPP.

## METHOD

### *Subjects*

Seventy-two experimentally naive male Sprague-Dawley rats (Taconic Farms, Germantown, NY), weighing 175–200 g when purchased, served as the subjects. Upon arrival at the laboratory, they were individually housed in standard hanging cages where food and water were always available. The colony room was maintained at 22°C with 12 h of artificial light daily (lights on at 0700 h).

### *Drugs*

Doses of MDMA HCl were 0.2, 2.0, 6.3 and 20.0 mg/kg. Morphine sulfate was tested at a dose of 8.0 mg/kg. This dose of morphine produces reliable CPPs in our apparatus (22) and, therefore, was used as a standard to assess these particular procedures. Physiological saline, the vehicle of both drugs, served as placebo. All injections were administered SC, 1 ml/kg.

### *Apparatus*

The procedures used 12 nearly identical alleys having two distinctive sides, separable by a removable wall. One side had black and white horizontal stripes and a floor of stainless steel rods running perpendicular to the length of the alley. The other side was grey and had stainless steel rods running parallel to the length of the alley. Each alley was housed in a sound-attenuating chamber equipped with a light over each half of the alley so that the level of refleted light on each side could be made nearly equal.

Each alley was balanced on a rod running perpendicular to the alley's length (centered through the top of the walls). When a rat was on one side of the alley, the alley tilted slightly to that side and completed an electrical circuit. Using this feature, the amount of time a rat spent in a particular side of the alley was tabulated automatically with the aid of a personal computer and data-acquisition software. The apparatus and general procedures have been described extensively elsewhere (22).

### *Procedure*

The day after their arrival at the laboratory, all rats began a 5-day schedule of handling. Each day, rats were weighed (as they were on every day of these procedures), placed in a cage on a cart (12 rats at a time, one rat/cage) and transported into an adjacent room containing the apparatus. Once in the room, each rat was handled briefly and returned to its home cage. All handling, conditioning and testing was performed between 0900 and 1300 h, i.e., during the lighted period of the light/dark cycle.

On Days 6 and 7, the rats were placed into their respective alleys with access to both sides, for 30 min. On Day 7, baseline preferences for a side (the side randomly designated as the side of putative conditioning prior to baseline) were recorded. Each alley was washed with a small concentration of a lemon-scented detergent in warm water and wiped dry before placing a rat in its alley. Across Days 8 and 9 no procedures were performed.

The rats were assigned to one of 6 groups (based on their baseline scores) with each group to receive a different kind of injection. Kinds of injections were then randomly assigned to each group. As a result, the groups were nearly equal or equal in terms of (a) baseline scores, $F(5,66)<1$, (b) number of subjects/group ($n=12$), and (c) number getting putative drug of conditioning on the grey or striped side of the alley.

On each day, across Days 10 to 12, the rats were weighed and injected with their respective drug of putative conditioning (saline, one of the four doses of MDMA, or morphine). Ten min later, each rat was confined in its side of putative conditioning for 30 min. On Day 13, all rats received injections of saline 10 min before being placed into the alternate side of the alley for 30 min.

On Day 14, there was a test during which each rat was placed in its alley with access to both sides (for 30 min) and the time spent on the side of putative conditioning was tabulated (the same procedure as baseline). After 2 days of no treatment, the procedure of (a) 3 daily sessions on the side of putative conditioning, (b) 1 day on the alternate side, and (c) a test day was repeated three more times, with two days of no treatment in between each 5-day cycle, for a total of 16 conditioning days and 4 tests.

### *Measures, Data Reduction and Statistics*

As mentioned, the time spent on a particular side of the alley was automatically tabulated. The scores were converted to the percentage of time spent on the side of putative conditioning. A score greater than 50% indicates that the rat spent more time on the side of putative conditioning.

Given that groups were matched on scores following baseline and that our previous research with these procedures and apparatus indicates that baseline scores are not significantly correlated with test scores, baseline scores in this instance can be ignored in assessing the effects of drugs. Unlike previous results assessing drugs with these procedures, an overall preference for the grey side of the alley did develop, $F(1,60)=34$, $p<0.0001$. This side preference was probably due to some slight difference in the lighting levels, with the grey side being somewhat darker. The factor of side did not, however, reliably interact with kind of drug administration, $F(5,60)=0.7$, $p>0.65$. Consequently, side of putative conditioning was ignored in the analysis.

The results of each individual test were similar, $F(3,180)=0.3$, $p>0.8$. Consequently, both the average score across tests and the scores of each test are indicative of drug effects. We chose to use the rats' mean score across tests as the data reflecting effects of the doses, but do comment on some slight differences in interpretation if only Test 4's scores are used. Consequently, the data conform to a one-way analysis of variance (ANOVA) of the six groups' mean test scores, i.e., the results of interest are associated with the main effect of kind of injection (saline, one of four doses of MDMA, or morphine). Student's *t*-tests, for independent measures, were used to make further between group comparisons.

## RESULTS AND DISCUSSION

Figure 1 depicts the mean scores for each group. The ANOVA revealed a reliable source of variance associated with the kind of injection, $F(5,60)=3.15$, $p<0.01$. A comparison of the control group's scores to those of the group which was treated with morphine, the standard drug, revealed that morphine produced a characteristic CPP, $t(22)=3.81$, $p<0.001$. This finding indicates that the procedures of this particular assessment met the criterion of producing an expected effect with a dose of a standard.

The *t*-tests for comparison of scores of each dose of MDMA to those of placebo yielded $t(22)$s $=1.78$, 2.84, 3.39 and 1.91 for the 0.2, 2.0, 6.3 and 20.0 doses, respectively. The *t*-values associated with the 2.0 and 6.3 doses of MDMA meet standards of statistical significance, both $p$s$<0.01$. The *t*-values associated with the 0.2 and 20.0 doses of MDMA only approach the conventional standard of statistical significance, $p=0.089$ and $p=0.069$, respectively.

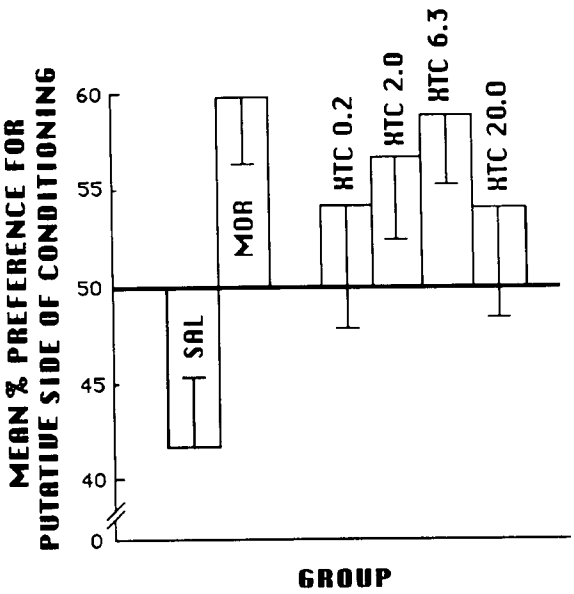


FIG. 1. Mean % of time on side of putative conditioning across the four tests of the procedure is depicted for each group. A score greater than 50% indicates a preference for the place where the effects of the injections in question were experienced. SAL refers to injections of saline, the vehicle of drugs. MOR refers to injections of 8 mg/kg doses of morphine sulfate. The numbers associated with MDMA are doses in mg/kg. The bars refer to standard errors of the means.

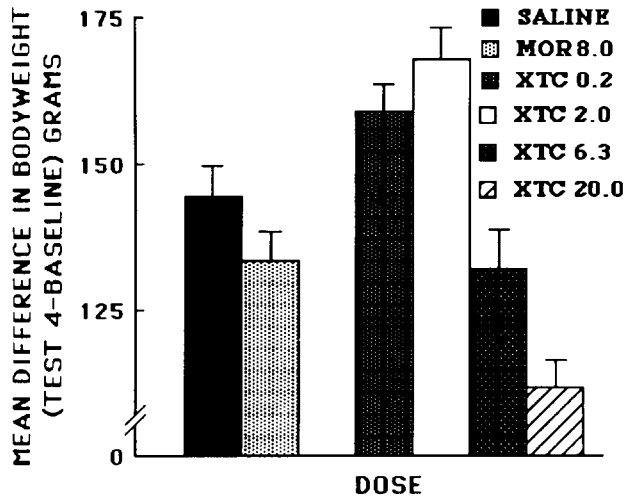


FIG. 2. Gain in weight, across the period of injections, is summarized. Periodically across the 29 days between baseline and Test 4, rats received 12 injections of either saline, a dose of morphine (MOR, 8 mg/kg), or one of four doses of MDMA (0.2, 2.0, 6.3 or 20.0 mg/kg). The gain in weight, therefore, of rats receiving saline are what would be expected with little or no intervention. The bars refer to standard errors of the mean.

An inspection of the data for each test indicates that a small shift across tests for the lowest and highest doses does appear even though the statistics indicate no differential effects across tests. Student's $t$-tests comparing these groups to the saline control at Test 4 reveal reliable differences, $t(22)$s = 3.2 and 3.04, $p$s<0.007. The lowest dose, being minimally effective, may require multiple pairings for a statistically significant CPP to emerge. The highest dose may have some initial aversiveness which tolerates with repeated dosing. If one takes into account only Test 4's results, MDMA produces a CPP across a wide range of doses.

If one analyzes the data for each side of putative conditioning (grey or striped) separately, the conclusion remains the same. For example, across tests, the mean control score for the striped side was 35.6% and the mean score for MDMA, 6.3 mg/kg, was 47.4%. The mean control score for the grey side was 47.5%, while the mean score for MDMA, 6.3 mg/kg, was 66.0%.

These results confirm that MDMA produces an effect that might be characterized as positive effect, an effect that might readily reinforce events leading to self-administration of MDMA. The positive affect was elicited across a fairly broad range of doses, even doses that might be considered large. Furthermore, the range of doses that produced a reliable CPP at Test 4 includes doses that did not lower thresholds for rewarding brain stimulation, giving further support for the utility of the CPP procedures in assessing a drug's liability for addiction. In addition, the positive effects produced by some doses were seen with the first test and did not diminish across repeated tests. For example, the mean score for Test 1 of MDMA, 6.3 mg/kg, was 58% and for Test 4, 61.2%. In other words, we did not see signs of tolerance to the positivity elicited by MDMA.

The fact that MDMA produced signs of positivity on the first test and the lack of tolerance seen across the four sets of administrations, all support the conclusion that MDMA has considerable liability for addiction. If MDMA, in the doses used here, produces damage to serotonergic systems, as some findings indicate [for a review, see (17)], it is doubtful whether those serotonergic systems are critical for MDMA's positivity, since we saw no signs of extinction across repeated tests.

Recently, it was hypothesized that MDMA's effects are temporally biphasic with serotonergic stimulation occurring during the first 30 min after injection and dopaminergic stimulation occurring sometime later, with peak levels of serotonin reached at 30 min, and dopamine, at 90 min (25). In this experiment, rats were conditioned between 10 and 40 min postinjection. This period would fall into the time where serotonergic activity would be peaking and dopaminergic activity would be relatively low. This is interesting since dopaminergic activity is likely to be critical to the establishment of a CPP (26). By manipulating the conditioning times to coincide with peak dopaminergic activity, even stronger MDMA-CPPs may be produced.

In this experiment, MDMA also affected the rats' body weights. A one-way ANOVA of the six groups' mean body weights at baseline indicated no reliable difference between groups, $F(5,71) = 0.40$, $p>0.8$. Further analyses across the 5 measures (baseline and 4 tests) revealed reliable main effects associated with the factors of Type of injecton, $F(5,66) = 7.93$; Days, $F(4,264) = 1720$; and, a reliable interaction between the two, $F(20,264) = 6.31$ (all $p$s<0.0001).

A summary of the results is presented in Fig. 2 as the mean difference between the body weights at Test 4 and Baseline. Student's $t$-tests, for independent measures, comparing the difference scores of the control group to each of the other groups indicated a reliably larger increase in body weight for the group which was treated with 2.0 mg/kg of MDMA, $t(22) = 2.62$, $p<0.02$, and a reliably smaller increase for the group treated with 20.0 mg/kg of MDMA, $t(22) = 4.60$, $p<0.0001$. The difference scores of the groups treated with the other doses of MDMA and with morphine were not reliably different from controls.

MDMA's multiple effects on body weights of rats having nearly unlimited access to food and water are unexpected. Data

from Experiment 2 lead to the suggestion that MDMA would dose-relatedly decrease body weight and, in this experiment, the highest dose did lead to a smaller gain in body weight compared to controls. Other research leads to the suggestion that stimulation of certain serotonergic receptors, either by direct agonist effects or reuptake inhibition, dose-relatedly decreases intake of food (4, 5, 13, 27). The increases in body weights seen with the 2.0 mg/kg dose of MDMA are, however, difficult to explain. In the case of fluoxetine's (a serotonin reuptake inhibitor) anorectic effects (13), there is a report of rebound feeding with the drug's metabolism (24), but also a report of no such compensatory effects (3). These data do, however, support the general conclusion that recreational drugs of abuse could produce perturbations in ingestive processes that may manifest themselves, among people, as disturbances in regulation of ingestion (18).

## EXPERIMENT 2

There are multiple reasons for studying MDMA's effects on intake of alcohol. There is the general idea that one drug of abuse is apt to promote the use of other drugs of abuse and that general notion needs to be assessed across a number of particular drugs. Additionally, there is the possibility that acute and long-term perturbations of serotonergic systems (as most likely occurs with injections of MDMA) might be particularly salient to propensity to take alcoholic beverages (6, 8, 16, 20, 23). Given these considerations, we assessed the effects of doses of MDMA on rats' intake of an alcoholic beverage using procedures previously used to assess morphine's effects [for a review, see (9)].

### METHOD

#### *Subjects*

The subjects of these procedures were 50 experimentally naive rats similar to those used in Experiment 1. Upon arrival at the laboratory, they were individually housed in standard hanging cages in the same colony room as the subjects of Experiment 1. Throughout these procedures, the rats had free access to food, but restricted access to water as described below. All procedures were performed in the rats' home cages.

#### *Drugs and Solutions*

These procedures involved the daily presentation of a sweetened ethanol solution (ES) and tap water to the rats. Each 100 g of ES contained 12 g of pure ethanol (E), 5 g of sucrose, and 83 g of tap water. Solutions were presented in glass bottles equipped with ball-point sipping tubes which substantially reduce spillage (7,19) and evaporation (19).

The assessment of propensity to take ethanol usually does not use a sweetened alcoholic beverage on the grounds that the propensity to take the beverage may be due to the sweetness, the ethanol, or to their interaction. The usual beverage used in this kind of assessment is ethanol in tap water. A careful consideration of the two alternatives (sweetened or plain), however, leads to the conclusion that the sweetened solution actually minimizes the factor of palatability. Regardless, however, of whether or not the sucrose-ethanol-water solution is less salient with respect to palatability (i.e., is more neutral in taste) than ethanol-water [which is bitter (11)], it is clear that rats take more of the sweetened solution. There is an advantage to assessing a drug's effects on propensity to take an alcoholic beverage when intake of the beverage is clearly sufficiently large to yield marked effects of ethanol.

The doses of MDMA tested were 0.0 (i.e., placebo), 0.2, 2.0, 6.3 and 20.0 mg/kg. Physiological saline, the vehicle of MDMA, served as placebo. All injections were administered subcutaneously, 1 ml/kg, 10 min before the presentation of fluids.

#### *Procedure*

Across the first 5 days at the laboratory, the rats had free access to water. Subsequently (Day 1), they were put on a daily regimen involving 22 h of fluid deprivation followed by a 2-h period (0900–1100 h) during which they were presented with a bottle containing ES and a bottle containing tap water. Under this daily regimen, rats typically take very little ES at first, but across the first 2–3 weeks they escalate their mean intake to about 2.0 to 2.5 g of pure E per kg of body weight (g/kg). At this point, the rats' daily intakes of E become stable [for a review, see (9)].

*Baseline phase.* Across Days 29–32, this particular group of rats took, on the average, 2.16 g/kg of E each day. The rats were then divided into 5 groups ($n = 10$ group) such that the mean g/kg intakes of the groups across Days 29–32 were nearly equal, $F(4,45) < 1$. Drug treatments (i.e., a dose of MDMA) were then randomly assigned to each group.

*MDMA administration phase.* Across the next 12 days (i.e., Days 33–44), the effects of MDMA were assessed. The rats which received the 20 mg/kg dose of MDMA took almost no fluids on the first two days of MDMA administration resulting in considerable weight loss. Therefore, across the remaining days of MDMA administration, this group of rats received an additional 1 h of access to water immediately after the 2-h session. This additional opportunity to drink seemed to prevent the excessive loss of weight that was characteristic of the first two days. The other groups were not given this additional access to water.

*Recovery phase.* Subsequent to the 12 days of injections, rats' intakes were measured for another 16 days. During this time, the rats of the 20 mg/kg group of MDMA were no longer allowed the additional h of water availability.

#### *Measures, Data Reduction and Statistics*

Beginning on the 25th day of the daily regimen, the rats' body weights and intakes were tabulated. Body weights were tabulated about 0.5 h before the session. The amounts of ES and water taken were also tabulated to the nearest 0.1 g and corrected for spillage (7). From these basic measures, the g/kg intakes of E and water were calculated.

Changing the amount of time that the 20 mg/kg of MDMA group had to take water across the last 10 days of dosing was an uncontrolled and potentially confounding variable. Therefore, the data of that group were not included in the formal analyses. Other analyses, which included that group's data, were performed and the conclusions drawn from those analyses do not differ from the conclusions drawn from the formal analyses.

Overall, the data conform to a 4 by 32 ANOVA having repeated measures with factors associated with Dose of MDMA and Days of the formal experiment (Days 29–60), respectively. However, to simplify the presentation of the results, the data were summarized in terms of 4-day means. Thus, the data conform to a 4 by 8 ANOVA having repeated measures with factors associated with Dose of MDMA and Blocks of 4-day means, respectively.

Since a reliable interaction term emerged, subsequent analyses were performed on each of the logical phases of the experiment, i.e., Baseline, MDMA administration, and Recovery phases. The overall ANOVA (across Baseline, Administration and Recovery) of the data associated with the g/kg intake of E revealed a reliable source of variance associated with the interaction between

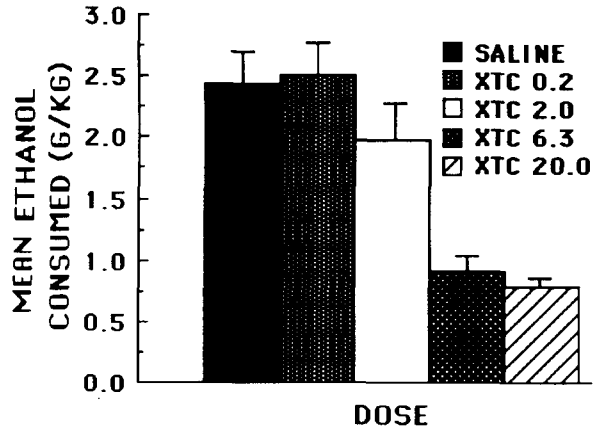


FIG. 3. Mean consumption of ethanol (g/kg) across the period of dosing is depicted. Prior to dosing, water-deprived rats were taking a mean of 2.2 g/kg pure E. Subsequently, they were divided into 5 groups each having nearly equal intakes of E. They were then given 12 daily injections of either saline or one of four doses of MDMA (0.2, 2.0, 6.3 or 20.0 mg/kg) 10 min prior to their 2-h drinking session. Intakes for the saline group were maintained at predosing levels, while the two highest doses of MDMA decreased ethanol intake. Bars refer to standard errors of the means.

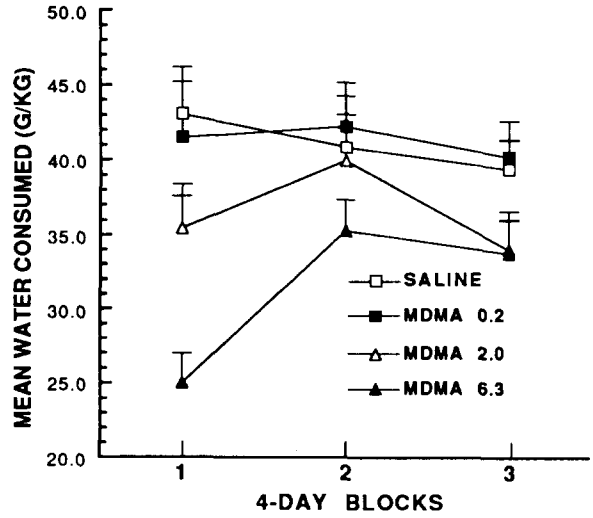


FIG. 4. Mean consumption of water (g/kg) for the 4 groups (saline control or one of 3 doses of MDMA) across the 3 blocks of MDMA administration are depicted. Prior to dosing these water-deprived rats were taking a mean of 45.7 g/kg water (13.5 g of water). Bars refer to standard errors of the mean.

Factors of Doses and Blocks, $F(21,252)=3.66$, $p<0.0001$. The data of the MDMA administration and Recovery phases conform, respectively, to 4 (Doses) by 3 (Blocks) and 4 by 4 ANOVAs having repeated measures. Subsequent analyses involved the appropriate one-way ANOVAs and Student's $t$-tests.

## RESULTS AND DISCUSSION

MDMA dose-relatedly decreased rats' mean g/kg intake of E and water, and body weight. During the Recovery phase, intakes of E and water returned to control levels in a couple of days. As a result, the groups which lost weight began to regain weight during this phase.

Analyses across the period of MDMA administration revealed that the groups took different amounts of E, $F(3,36)=9.82$, $p<0.0001$. The ANOVA also revealed that across the 3 blocks of MDMA administration the groups' mean intakes were stable ($p>0.75$), and that there was no differential pattern of intakes across groups ($p>0.13$). Therefore, we further collapsed the data of each rat into a single mean score reflecting its mean g/kg intake across the period of MDMA administration (see Fig. 3) and compared the mean intakes of the 0.0 mg/kg (i.e., control) group with each of the other groups. Student's $t$-tests, for independent measures, revealed that the 0.2 and 2.0 mg/kg doses of MDMA did not reliably modify intake of E as compared to controls ($ps>0.8$ and 0.2, respectively). The 6.3 mg/kg dose of MDMA did reliably decrease intake of E as compared to controls, $t(18)=5.48$, $p<0.0001$.

The analysis of the data of the Recovery phase with measures of intake of E failed to reveal any reliable sources of variance. In brief, the rats' intakes of E returned to the level seen at baseline.

Prior to dosing, groups' mean intakes of water were roughly equal, $F(3,36)=0.27$, $p>0.8$. During the MDMA administration phase, groups took different amounts of water, $F(3,36)=4.54$, $p<0.009$. In contrast to intake of E, the mean water intakes were not stable across the 3 blocks during which MDMA was given, $F(2,72)=4.56$, $p<0.02$.

The data associated with water intake across MDMA administration blocks are depicted in Fig. 4. The low doses of MDMA produced almost no shift in intake of water while the 6.3 mg/kg dose reduced intakes, especially during the 1st 4-day block, as indicated by the reliable interaction term of the ANOVA of water intake during dosing, $F(6,72)=3.89$, $p<0.003$. Also, recall that the 20 mg/kg dose of MDMA reduced drinking levels to nearly zero during the period just after its administration.

During the Recovery phase, the rats whose water intakes were previously suppressed drank more water. By the last block of days, however, intakes of water were nearly the same across all groups, $F(4,45)=0.2$, $p>0.9$.

The rats of Experiment 1, subsequent to their CPP procedures, were put on a similar daily regimen of those of Experiment 2. Recall that some rats had received 12 doses of 20 mg/kg MDMA. We observed no reliable effects associated with history of MDMA on daily intake of ES (measured on Days 1–8 and on Days 18–21 of being maintained on the daily regimen). These observations confirm those associated with the recovery phase of this experiment, i.e., a history of MDMA does not produce a reliable change in daily intake of a sweetened alcoholic beverage.

## GENERAL DISCUSSION

The results indicate that MDMA produces a positive affective state across a number of doses, but does not potentiate intake of an alcoholic beverage. In fact, MDMA dose-relatedly decreases intake of the alcoholic beverage (and water). This is in contrast to morphine and some other opioids which produce strong CPP's (2,22) and potentiate intake of this as well as other alcoholic beverages (9). The potential generalization that any dose of an agent producing signs of positive affect is one that increases propensity to drink an alcoholic beverage is not correct.

These findings extend previous work (10) using MDMA by indicating that MDMA's potential for positive affect is seen across a rather large span of doses including those producing states interfering with even a strong motivation to drink. Since MDMA is a serotonergic agonist (21), a reduction in sweetened ES intake

might be predicted (6, 8, 16, 20, 23) and that was what was seen. The lowest effective dose needed to produce a CPP did not, however, produce reliable decrements in alcohol consumption.

In Experiment 1, when MDMA was given periodically, it both incremented and retarded, depending on dose, gain in body weights when food and water were available. Therefore, a side effect of MDMA might be to produce abnormal shifts in body weights.

Rats getting MDMA looked almost indistinguishable from rats getting saline except for a foam developing at the mouth with the 20 mg/kg dose. Yet the rats with the highest doses did not drink when given the opportunity despite severe water deprivation. An agent that produces powerful affective effects and interferes with a basic motivation such as drinking when thirsty would seem to be one with an extraordinary impact.

Even though we had no direct measures of neurotoxicity, the doses and administrations used here almost assuredly produced neurotoxicity of serotonergic systems similar to those measured by others (17). Despite the potential for neuronal damage, the rats maintained strong CPPs with continued conditioning, and showed no long-term differences in E intake compared to controls. The fact that there were no postdosing effects on intake of E does not support the idea that perturbations of serotonergic systems leads to modified intake of alcohol.

ACKNOWLEDGEMENTS

We thank Jean Bestle and Elizabeth Osganian for their help in preparing the manuscript, Dr. Michael Kalsher for the use of his computer, and Michael Nichols for his assistance with the data collection. This work was supported, in part, by Grant DA 04440 from the National Institute on Drug Abuse (NIDA). MDMA was provided by the NIDA Drug Supply Program: Research Technology Branch.

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