The Motivational Effects of 3, 4-Methylenedioxyamphetamine on Responding Maintained by a Progressive-Ratio Schedule of Water Delivery

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THE MOTIVATIONAL EFFECTS OF 3,4-METHYLENEDIOXYMETHAMPHETAMINE ON RESPONDING MAINTAINED BY A PROGRESSIVE-RATIO SCHEDULE OF WATER DELIVERY

by

Sean P. Laraway

A Thesis
Submitted to the
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in partial fulfillment for the
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I would first like to thank my committee members. From the start, Dr. Jack Michael has been a fine mentor and a good friend. I owe special thanks to Dr. Alan Poling, who has taught me more than I can recount in this small space. As a scientist, he has shown me the value of clear thinking, confident humility, and cool perseverance in the face of adversity. Finally, I would like to thank Dr. Lisa Baker, who challenged me in the classroom and helped me in the laboratory. Thank you all.

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Through the hard work and devotion of my parents Charles and Susan Laraway, I was fortunate enough to obtain undergraduate and graduate degrees. I would also like to thank my brother Scott Laraway for his support. I am grateful to my grandmother Genevieve Werdehoff for her many years of love. Finally, I would like to thank my extended family Mark, Karin, Sophia, and Lukas Snyderski for the love, support, and festivity they have given me during graduate school. I feel lucky to have you all in my life.

Finally, I would like to thank my wife Dr. Susan Snyderski, a competent and accomplished scientist in her own right. Her patience, love, and intellectual input have made these last few years the best years of my life. I love you and am thrilled to enter the next phase in our life together. Thank you.

Sean P. Laraway
Relative to their reinforcing and discriminative functions, the establishing operation (EO) function of drugs has received little attention from behavioral pharmacologists. This study investigated in rats the EO function of 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy) using a progressive-ratio (PR) 2 schedule of water delivery. Relative to vehicle control levels, Lower doses (1.0 and 1.8 mg/kg ip) had no effects, whereas the higher doses (3.2, 5.6 mg/kg ip) significantly decreased breaking points. Changes in the level of water deprivation significantly changed breaking points. In contrast to previous research, this study found no evidence that MDMA functioned as an EO for water. These results, along with findings from other studies using PR schedules, emphasize the need for caution when interpreting drug-induced changes in breaking points.
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Identification of behavioral mechanisms of drug action remains a primary goal of behavioral pharmacology (Poling, 2000; Thompson & Schuster, 1968). Such behavioral mechanisms include a drug's operant and respondent functions and its capacity to modulate the behavioral control of other events. When investigating behavioral mechanisms of drug action, researchers have concentrated primarily on drugs' reinforcing and discriminative stimulus functions. Although these functions are important for understanding drug effects, drugs can affect behavior in other ways, such as by altering the reinforcing or punishing effectiveness of behavioral consequences (e.g., Griffiths, Wurster, & Brady, 1981; Houser, 1978; Laraway, Snycherski, Byrne, & Poling, 2000; Levine & Billington, 1989; Mello, Mendelson, & Kuehnle, 1982; Miller, 1956, 1957; Northrup, Fusilier, Swanson, Roane, & Borrero, 1997; Poling, 1986). That is, drugs may function as motivational variables. Researchers have not systematically investigated drug effects on the effectiveness of reinforcers and punishers; the relative paucity of research on these effects represents a considerable gap in our knowledge.

One conceptual development that might facilitate research into the motivational effects of drugs is the emergence of an operant approach to motivation, primarily from the writings of Michael (1982, 1983, 1988, 1993a, 1993b, 2000). Michael reintroduced, extended, and popularized the establishing operation (EO) concept, first used by Keller and Schoenfeld (1950), and then by Millenson (1967), to refer to variables that "established" events as effective consequences. The EO concept represents an environment-based theory of motivation that is well-integrated with other operant concepts. Interestingly, few behavioral
pharmacologists seem to have been influenced by Michael's work, for they have made little use of the establishing operation concept, though there are some exceptions (e.g., Northrup et al., 1997; Poling, 1986; Poling & Byrne, 2000).

Building on Michael's previous work on the EO concept, Laraway, Snycherski, Michael, and Poling (2002) extended and refined behavior-analytic motivational concepts and terminology. These authors termed all variables that have motivational effects *motivative operations* (MOs), which they defined as environmental events, operations, or stimulus conditions that affect behavior by altering (a) the effectiveness of reinforcers or punishers (the *value-altering effect*) and (b) the characteristics of operant response classes related to those consequences (the *behavior-altering effect*). The *value-altering effect*, as a generic term, subsumes the following specific effects of MOs: (a) the reinforcer-establishing effect, (b) the reinforcer-abolishing effect, (c) the punisher-establishing effect, and (d) the punisher-abolishing effect. Based on these value-altering effects, Laraway et al. (2002) identified two basic MO subtypes: establishing operations (EOs) and abolishing operations (AOs), which make consequences more or less effective, respectively. The *behavior-altering effect*, as a generic term, subsumes two effects of MOs: (a) the evocative effect and (b) the abative effect (see Laraway, Snycherski, Michael, & Poling, in press). The evocative effect represents an increase, and the abative effect represents a decrease, in a measure of some characteristic of an operant response (e.g., response rate, resistance to change, breaking points under progressive-ratio schedules).

As an approach to motivation, the MO concept possesses some desirable features that should expedite investigations into drug effects and the variables that modulate those effects. First, the MO concept provides a consistent taxonomy of
variables that influence the effectiveness of reinforcers and punishers. Researchers have long recognized that the effectiveness of consequences fluctuates across time and settings (Millenson, 1967), and MOs are among the variables that influence these fluctuations. Second, unlike traditional motivational concepts (e.g., needs, craving), MOs are measured at the same level of analysis as the behavior of interest and are described in clear relation to other operant controlling variables. This tight integration of the MO concept with other behavioral concepts allows behavioral pharmacologists to describe the motivational effects of drugs and other events without relying on unobservable or poorly defined processes or events (Sundberg, 1993), such as cravings, which often fail to correlate with the behaviors of interest (Poling, in press) and which have no clear connection to operant concepts.

Beyond its significance for a general understanding of drug effects, the MO concept has considerable importance for drug-abuse treatment research, which frequently involves searching for variables that reduce the reinforcing efficacy of abused drugs. Many pharmacotherapies for drug abuse function as motivational variables (a) by reducing the reinforcing effectiveness of abused drugs (e.g., methadone therapy for heroin abuse) or (b) by changing the function of the abused drug from reinforcing to punishing (e.g., disulfiram therapy for alcohol abuse) (Bigelow, Stitzer, & Liebson, 1986; Hall, Clark, & Sees, 1996; Schuster, 1986). In terms of the MO concept, pharmacotherapies that operate as in (a) function as AOs for drug reinforcers, while those that operate as in (b) simultaneously function as AOs for drugs' reinforcing effects and EOs for their punishing effects. By providing a consistent description of variables having common behavioral effects, the MO concept may help guide research on the neurochemical mechanisms that underlie these effects, thereby increasing the power and scope of our behavioral interventions for
drug abuse. As Johanson (1990) noted: "an understanding of the variables affecting
the reinforcing effects of drugs [i.e., motivative operations] is of paramount
importance in developing effective prevention and treatment interventions" (p. 385).

Drug-abuse researchers, healthcare professionals, and government agencies
have demonstrated increasing concern over the growth in the use of the popular
“club drug” (±)3,4-methylenedioxymethamphetamine (MDMA, ecstasy, E),
particularly by young people at dance clubs or raves (McDowell & Kleber, 1994;
Schwartz & Miller, 1997). The apparent growth in MDMA use makes a complete
understanding of the many behavioral effects of this drug critical. In addition to its
reinforcing and discriminative functions (Steele, McCann, & Ricaurte, 1994),
MDMA appears to function as an EO for water in a manner similar to water
deprivation. For example, Rezvani, Garges, Miller, and Gordon (1992) utilized a
choice procedure to investigate the effects of acute and subchronic injections of
MDMA on ethanol preference in two strains of ethanol-preferring rats [i.e., Fawn-
Hooded (FH) and ethanol-preferring (P) rats]. In this study, all rats received free
access to food, water, and a 10% (v/v) ethanol solution in their home cages, and
their daily intake of food, water, and ethanol solution was recorded. In the first
experiment, rats received a single injection of either saline solution or 5.0 mg/kg
MDMA after ethanol and water intake stabilized. Results of the first experiment
indicated that for both strains of rats a single injection of 5.0 mg/kg MDMA
significantly reduced mean ethanol intake and significantly increased water
consumption, relative to baseline (no injection) and vehicle conditions. Moreover,
in both strains of rats 5.0 mg/kg MDMA significantly reduced the proportion of
ethanol intake to total fluid intake, an index of ethanol preference.
In a second experiment, Rezvani et al. (1992) administered daily injections of either MDMA or saline for three consecutive days to both strains of rats. All other aspects of the second experiment were similar to those in the first experiment. In the second experiment, three-day administration of 5.0 mg/kg MDMA significantly reduced ethanol intake in FH rats on each day. No significant changes in food or water consumption were found with this strain. As was found with the FH rats, the subchronic administration regimen significantly reduced ethanol intake in the P rats. In contrast to the FH rats, however, the P rats exhibited a significant increase in water intake for all three days and a significant decrease in food intake for the first two days. The changes in food, water, and ethanol consumption due to MDMA administration seen in this study can be interpreted as reflecting changes in the reinforcing effectiveness of these stimuli (Higgins, Bickel, & Hughes, 1993). Hence, in this study MDMA appeared to have functioned as an EO for water and as an AO for food and ethanol, and these functions depended, in part, on genetic variables. It is not surprising that MDMA abolished the reinforcing effectiveness of food, given the drug is structurally related to the amphetamines, which typically reduce food consumption.

Byrne, Baker, and Poling (2000) examined the effects of MDMA on response acquisition with immediate and delayed water delivery. Byrne et al. found that when water was delivered under a fixed-ratio (FR) 1 schedule, rats that received MDMA made more responses and earned more water deliveries than did rats that received vehicle. To the extent that more robust acquisition provides evidence of increased reinforcing effectiveness (Millenson, 1967), Byrne et al.'s results suggest that MDMA engendered better acquisition of lever pressing by altering the reinforcing effectiveness of water, although this effect depended on the delay to water delivery.
MDMA could exert its motivational effects through several possible physiological mechanisms. In rats, MDMA has been shown to induce hyperthermia, increase evaporative water loss, and increase salivation (Green, Cross, & Goodwin, 1995; Gordon, Watkinson, O'Callaghan, & Miller, 1991; Spanos & Yamamoto, 1989). These physiological effects, alone or in combination, could increase the reinforcing value of water.

In sum, the results of Rezvani et al. (1992) and Byrne et al. (2000) suggest that, similar to water deprivation, MDMA may function as an EO for water delivery. However, as Miller (1956, 1957) noted, the motivational effects of drugs and other events should be assessed in a variety of ways to prevent misleading generalizations from results that depend on the specific procedure used to index reinforcing effectiveness. Due to the importance of characterizing MDMA's effects and the relative paucity of research on drug MOs, the present study examined further the possible motivational (i.e., EO) function of MDMA for water using a well-accepted assay of reinforcing effectiveness, the progressive-ratio (PR) schedule. To our knowledge, no studies have examined the effects of MDMA on responding reinforced by water delivery arranged under a PR schedule.

Progressive-ratio schedules require subjects to execute a systematically increasing number of responses for each successive reinforcer (Hodos, 1961). For example, under a PR 2 schedule of water delivery, the number of responses the subject must emit in the session begins at two and is incremented by two responses each time the subject earns a water delivery. Thus, under a PR 2 the first 10 ratios in a given experimental session would be 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20. The response requirement continues to increase until the subject ceases to respond for some specified period, usually between 5 and 15 minutes, at which time the
session terminates (e.g., Hodos, 1961; Hodos & Kalman, 1963; Thomas, 1976). The number of responses in the last completed ratio of the session, termed the breaking point, serves as the primary measure of reinforcing value under the PR schedule (Hodos, 1961; Stewart, 1975). The breaking point reflects the threshold at which the organism will no longer work on the schedule given the current response requirements or, alternatively, the point at which the scheduled consequence fails to maintain performance. Progressive-ratio schedules appear to provide a quantitative index of reinforcing effectiveness, with effective reinforcers defined as those that maintain relatively high breaking points (Hodos & Kalman, 1963; Lattal, 1991). If MDMA increases the reinforcing effectiveness of water, and if PR schedules assess reinforcing effectiveness, as is commonly asserted (e.g., Hodos, 1961; Hodos & Kalman, 1963; Katz, 1990; Stafford, LeSage, & Glowa, 1998), breaking points under a PR schedule should increase when MDMA is administered to rats.

METHOD

Subjects

Five experimentally naive male Sprague-Dawley rats (Charles River, Portage, MI), approximately 50 days old at the beginning of the study, served as subjects. Rats were housed individually in plastic cages (24 cm long x 31.5 cm wide x 21 cm high) located in a colony room maintained on a 12-hr light/12-hr dark schedule and kept at a relatively constant temperature (20-22°C). Throughout the study, rats had free access to food in their home cages.

Apparatus

All experimental sessions were conducted in operant conditioning chambers, 28 cm long x 21 cm wide x 21 cm high (Med Associates, St. Albans, VT). Each operant chamber contained a single response lever located 7 cm above the floor on
either the right or left side of the front response panel. An aperture located in the middle of the response panel allowed access to a dipper that provided 0.1 ml of tap water. An overhead 28-V house light provided ambient illumination throughout each experimental session. Each chamber was housed in a sound- and light-attenuating shell to which masking noise and ventilation were supplied. All experimental events were controlled and recorded by MED-PC software and instrumentation (Med Associates, St. Albans, VT, DOS v2.0) operating on an IBM-compatible personal computer.

Behavioral Procedure

All rats were water deprived for 24 hr prior to one 1-hr dipper-training session. Dipper training sessions entailed delivering water for 4 s under a variable-time 60-s schedule. Under this schedule, 4-s water deliveries occurred randomly after an average interval of 60 s, independent of the rats' behavior. All rats were observed to drink from the dipper by the end of the session. Following the dipper-training session, rats received lever-press training under an FR 1 schedule of water delivery. Before the beginning of lever-press training, rats were randomly assigned a lever position (i.e., left or right). Each rat received FR 1 lever-training until it made at least 100 lever-press responses per session in two consecutive training sessions.

After the second training session, the FR 1 schedule was changed to an arithmetically progressing PR 2 schedule of water delivery, which was in effect for the remainder of the study. Under this schedule, rats earned a 4-s water delivery upon completion of a response ratio that began at two and was progressively incremented by two responses after each successive water delivery. Experimental sessions ended after 1 hr or when a rat ceased to respond for 5 consecutive minutes.
(i.e., the breaking-point criterion), whichever occurred first. The 5-min breaking-point criterion was only in effect after rats earned their first water delivery. This was done because previous research suggested that MDMA suppresses responding early in experimental sessions, with increased responding occurring later (Byrne et al., 2000).

Following experimental sessions, rats were returned to their home cages and were given free access to water for 30 min. Sessions were conducted five days per week, at about the same time each day. After a rat's breaking point was stable for 10 consecutive sessions, the pharmacological procedures began. Stability was determined by calculating the mean breaking point for the first 5 sessions (sub-mean 1), the last 5 sessions (sub-mean 2), and the entire block of 10 sessions (overall mean). The difference between the two sub-means was divided by the overall mean and multiplied by 100, and the data were considered stable if the resulting percentage was less than 10 (cf. Perone, 1991). After the pharmacological procedures began, the stability criterion changed such that four stable sessions were required between injections. During this time, stability was assessed by visual inspection of graphed breaking points and was defined as the absence of increasing or decreasing trends across the previous four sessions.

Pharmacological Procedure

When a rat's responding under the PR schedule was stable, the rat received four vehicle injections in order to acclimate it to injection procedures. These vehicle injections were administered according to a BBBBCC design where B represents baseline (no injection) sessions and C represents vehicle control (saline injection) sessions. Upon achieving at least four days of stability after the fourth vehicle injection, an acute dose-response determination was initiated for that rat.
During this determination, each rat received four doses of MDMA increased in quarter-log units (i.e., 1.0, 1.8, 3.2, and 5.6 mg/kg). Drug injections were given according to a BBBBCD design, where B represents baseline sessions (no injection), C represents vehicle control sessions (saline injection), and D represents drug sessions (drug injection). Each dose was administered twice, and doses were administered in random order. Doses were chosen on the basis of those that appeared to be behaviorally active in rats in a prior study from this laboratory (Byrne et al., 2000).

**Water-deprivation Control Procedure**

To determine the sensitivity of the PR 2 schedule to a known motivational variable, the level of water deprivation of each rat was manipulated at the end of the pharmacological procedures. The logic of this control procedure was that if MDMA increases the reinforcing effectiveness of water, the drug should have effects similar to changes in the level of water deprivation (cf. Thompson, 1972a, b). Following the pharmacological procedures, rats were returned to baseline conditions (i.e., 22.5 hrs of deprivation under the PR 2) for 10 days. At the end of this baseline phase, rats received continuous free access to water in their home cages (i.e., 0-hr deprivation), which should have reduced the reinforcing effectiveness of water. After several PR 2 sessions at 0-hr water deprivation, 4 of 5 rats (Rats 1, 3, 4, and 5) were returned to a 22.5 deprivation regimen, after which they were tested at 46 hrs of deprivation. Due to time constraints, Rat 2 was tested at 46 hrs of water deprivation without the intervening baseline sessions. This minor difference in procedure had no discernible effects on performance.

**Drug**

MDMA (National Institutes on Drug Abuse, Rockville, MD) was dissolved in
sterile 0.9% saline solution prepared at an injection volume of 1 ml/kg in sterile vials and injected intraperitoneally (ip) with a sterile syringe 15 min prior to behavioral testing. Following injections, rats remained in their home cages until placed in experimental chambers for the start of test sessions.

Data Analysis

Breaking points and overall response rates were recorded for each session. The breaking point was defined as the last ratio completed before the session ended. Response rates were computed by dividing the number of responses by the total session time. For all rats, dependent measures for all conditions represent the mean value of experimental sessions under those conditions. For each rat, the means for breaking points and response rates were based on eight sessions for vehicle, two sessions for each drug dose, and five sessions for 0-hr deprivation. For each rat, values for the 46-hr deprivation condition represent data from one session. All data are expressed as the percent of vehicle control data.

RESULTS

For all rats, sessions usually ended because rats ceased to respond for five consecutive minutes (i.e., rats met the breaking-point criterion). Treatment-induced changes in breaking points generally were accompanied by similar changes in response rates in all rats. The one exception is 1.8 mg/kg MDMA, which had no effect on the mean breaking point but which decreased the mean response rate. Figure 1 depicts group mean (± SEM) breaking points for each treatment condition. Group data are presented because they adequately represent data from individual rats. Group mean response rates (standard deviations in parentheses) were 7.9 (5.0), 154.7 (38.4), 82.6 (45.0), 58.7 (52.1), 8.0 (9.4), and 4.5% (6.1%) for 0-hr deprivation, 46-hr deprivation, 1.0, 1.8, 3.2, and 5.6 mg/kg MDMA,
respectively.

Figure 1. Means (± 1 SEM) for breaking points for five rats as a group, for all experimental conditions. Data are presented in terms of percent vehicle control. The dashed line indicates control level of responding (i.e., 100%). Points with error bars that do not overlap are significantly different.

*p < .05; **p < .01
The effects of treatment conditions on breaking points were assessed with a one-factor repeated-measures analysis of variance (RM ANOVA) with the degrees of freedom adjusted according to the Giesser-Greenhouse “conservative” method (Huitema, 1980). Results of the RM ANOVA ($\alpha = .05$) revealed significant differences in breaking points across treatment levels, $F(1, 4) = 25.05$, $p = .0075$, $r^2 = .78$. To identify significant differences between treatment conditions, pairwise comparisons using Tukey HSD post-hoc tests were conducted on mean differences in breaking points between the two deprivation conditions and between each condition and vehicle control. Table 1 presents the results of these post-hoc tests and their associated 95% simultaneous confidence intervals; obtained test statistics were compared to critical values of the Studentized range statistic, $q(7, 24) = 4.54$ and 5.54, for $\alpha = .05$ and $\alpha = .01$, respectively.
Table 1

Tukey HSD Post-Hoc Tests and 95% Simultaneous Confidence Intervals on Mean Differences in Breaking Points

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Mean Difference</th>
<th>q</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>46 hr vs. 0 hr</td>
<td>199.8%</td>
<td>13.95**</td>
<td>(134.8, 264.8)</td>
</tr>
<tr>
<td>46 hr vs. Vehicle</td>
<td>119.2%</td>
<td>8.32**</td>
<td>(54.2, 184.2)</td>
</tr>
<tr>
<td>0 hr vs. Vehicle</td>
<td>-80.6%</td>
<td>-5.63**</td>
<td>(-145.6, -15.6)</td>
</tr>
<tr>
<td>1.0 mg/kg vs. Vehicle</td>
<td>-0.8%</td>
<td>-0.06</td>
<td>(-64.8, 64.2)</td>
</tr>
<tr>
<td>1.8 mg/kg vs. Vehicle</td>
<td>1.4%</td>
<td>0.10</td>
<td>(-63.6, 66.4)</td>
</tr>
<tr>
<td>3.2 mg/kg vs. Vehicle</td>
<td>-77.6%</td>
<td>-5.42*</td>
<td>(-142.6, -12.6)</td>
</tr>
<tr>
<td>5.6 mg/kg vs. Vehicle</td>
<td>-77.4%</td>
<td>-5.41*</td>
<td>(-142.4, -12.4)</td>
</tr>
</tbody>
</table>

Note: Mean differences in breaking points are presented in terms of percent vehicle control. These differences represent the effects of the first condition compared to those of the second condition.

*p < .05. **p < .01

As expected, breaking points after 46 hrs of deprivation were substantially higher than after 0 hrs of deprivation. Compared with vehicle data, 46-hr deprivation increased, and 0-hr deprivation decreased, mean breaking points. The effects of 1.0 and 1.8 mg/kg MDMA were inconsistent across rats. For three of five rats, 1.0 mg/kg had no effect on mean breaking points, but for the other two rats, this dose slightly increased (Rat 2) and slightly decreased (Rat 4) the mean breaking points, relative to vehicle. For Rats 1, 2, and 3, 1.8 mg/kg slightly
increased mean breaking points above those from vehicle sessions. In contrast, this
dose produced large decreases in mean breaking points for Rats 4 and 5. The two
highest doses, 3.2 and 5.6 mg/kg, decreased mean breaking points in all rats. No
significant increases in breaking points were associated with any dose of MDMA.

Direct observation after MDMA administration revealed that rats remained
active inside the experimental chamber, regardless of dose. Following
administration of 3.2 and 5.6 mg/kg, all rats exhibited signs of the serotonin
syndrome, including piloerection, head weaving, increased activity, and low body
posture (Green et al., 1995). Despite the clear disruption in PR performance
following administration of the two highest doses, this disruption was not due to
motoric impairment.

DISCUSSION

One purpose of this study was to evaluate further the behavioral effects of
MDMA, specifically its motivational effects. Contrary to our hypothesis, the present
study found no evidence that MDMA increased the reinforcing effectiveness of water
(i.e., functioned as an EO). If, as researchers generally assume, breaking points
provide a measure of reinforcing effectiveness (e.g., Hodos, 1961; Hodos & Kalman,
1963; Stafford et al., 1998), the present data suggest that lower doses of MDMA had
no effect on the reinforcing effectiveness of water, while higher doses abolished its
effectiveness. These results are inconsistent with those of other studies (Byrne et
al., 2000; Rezvani et al., 1992), which reported increases in the reinforcing
effectiveness of water following administration of the same doses of MDMA that
abated responding in this study. This discrepancy in results was not due to the
insensitivity of the PR 2 schedule to fluctuations in the reinforcing effectiveness of
water because changes in the level of water deprivation produced corresponding
changes in breaking points.

Other studies utilizing PR schedules have found similar discrepancies between the effects of drugs on breaking points and the characteristic motivational effects of these drugs. For example, Thompson (1972a), Schulze and Paule (1990), and Thomas (1976) found that low to moderate doses of d-amphetamine generally increased breaking points for food, even though the drug has well-known anorectic effects under other conditions (i.e., it reduces the reinforcing effectiveness of food and decreases responding for food). Similar results have been obtained with cocaine, another stimulant drug that typically has anorectic effects (Jones, LeSage, Sundby, & Poling, 1995). Moreover, studies examining the behavioral effects of opioid agonists, which typically increase food intake, have found that these drugs decrease breaking points under PR schedules, although subjects may develop a degree of tolerance to this effect (Jarema, Macomber, LeSage, & Poling, 1999; Macenski, Schaal, Cleary, & Thompson, 1993; Poling, LeSage, Roe, & Schaefer, 1996).

The data from the present study, along with the findings of previous studies, call into the question the notion that PR schedules provide a direct indication of how drugs affect the reinforcing effectiveness of other stimuli. As Jones et al. (1995) noted, “it should not be automatically assumed that drug-induced changes in PR breaking points provide an uncontaminated index of the relative effectiveness of the scheduled reinforcer” (p. 530). Schedule-controlled behavior is complexly determined, and drugs may affect such behavior through a variety of behavioral mechanisms (McKearney & Barrett, 1978; Poling, Byrne, & Morgan, 2000). For example, MDMA may increase the relative reinforcing effectiveness of motor activity, thereby abating behavior maintained by other reinforcers. This seems possible given: (a) the drug’s widespread use at dance clubs and rave parties, where
users may dance for extended periods of time, to the exclusion of other, possibly reinforcing, activities (Green et al., 1995; McDowell & Kleber, 1994; Schwartz & Miller, 1997); and (b) the increase in the reinforcing effectiveness of activity produced by other drugs with stimulant properties (e.g., Northrup et al., 1997). Regardless of MDMA's specific behavioral mechanism of action, converging data from several studies confirm the need for caution when interpreting the effects of drugs on responding maintained by PR schedules.

Although we failed to find clear evidence for MDMA's motivational effects, the present study has value for two reasons. First, this study provides more information regarding the behavioral effects of an increasingly abused club drug, MDMA. Second, this study examined the EO function of a drug. To our knowledge, only one other study has explicitly investigated a drug EO (i.e., methylphenidate, Northrup et al., 1997). Because drugs can function as motivational variables and drug effects can be modulated by them, such variables deserve increased attention by behavioral pharmacologists (Snycerski, Laraway, & Poling, 2000). The MO concept may be of value in guiding such research. Failure to investigate motivational variables' effects on behavior "leaves a gap in our understanding of operant functional relations" (Michael, 1993b, p. 191), preventing us from making complete and accurate behavioral assessments (Sundberg, 1993). Behavior analysts' application of Michael's general approach to motivation has proven useful in both theory and practice (see, for example, Agnew, 1998; Hall & Sundberg, 1987; Iwata, Smith, & Michael, 2001; McGill, 1999; Laraway et al., 2000; Olson, Laraway, & Austin, in press; Wilder & Carr, 1998). Given these successes, and the importance of other operant concepts for understanding drugs' behavioral effects (Branch, 1991; Byrne & Poling, 2000; Falk, 1996; Johanson, 1978), behavioral
pharmacologists' adoption of the MO concept will likely improve our behavioral analyses of drug action.
Appendix A

Protocol Clearance From the Institutional Animal Care and Use Committee
WESTERN MICHIGAN UNIVERSITY
YEARNLY RENEWAL FORM APPLICATION TO USE
VERTEBRATE ANIMALS FOR RESEARCH OR TEACHING

GENERAL INFORMATION: Fill in all appropriate information

Alan Poling PSY
Principal Investigator/Instructor Department Campus Phone

Sean Laraway PSY
Co-Principal/Student Investigator Department Campus Phone

Title of Project/Course The Effects of MDMA on Rats Responding Under a Progressive-Ratio Schedule Of Water Delivery

PRINCIPAL INVESTIGATOR/INSTRUCTOR DECLARATION
I assure that I have obtained IACUC approval prior to implementing this project and that there are no changes in the protocol submitted in the original application to use vertebrate animals for research or teaching. I understand that if at any time changes are made in the use of animals as described in the original application, a letter or amended protocol must be filed for review. I assure that the activities do not unnecessarily duplicate previous experiments.

Signatures:

Principal Investigator/Instructor

Co-Principal/Student Investigator

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE APPROVAL

PLEASE MAIL COMPLETED APPLICATION TO:
Research Compliance Coordinator
Western Michigan University
327E Walwood Hall
Kalamazoo, MI 49008
(616) 387-8293

NOTE: It is the responsibility of the Principal Investigator to obtain the signature of any Co-Principal/Student Investigators.
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