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An analysis of the utility of differential outcome procedures in drug discrimination research

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In differential outcomes procedures, the correlation of unique reinforcers with distinct discriminative stimuli can decrease the amount of time needed for response acquisition and improve terminal accuracy of responding. The drug discrimination assay is widely used to categorize psychoactive drugs as similar or dissimilar and to describe underlying neurochemical changes associated with drug administration. Because the drug discrimination assay relies heavily upon initial response acquisition and continuing terminal accuracy, a procedure successful at shortening acquisition time and improving terminal accuracy would be beneficial. The present studies examined differences in acquisition of drug stimulus control between rats exposed to differential outcome procedures and rats exposed to the outcomes, in a non-systematic way, in two experiments. The first experiment examined acquisition of control by (±)-3,4-methylenedioxymethamphetamine (MDMA), D-amphetamine and saline; the second examined control by MDMA, (+)-lysergic acid diethylamide (LSD) and saline. Neither initial acquisition nor terminal accuracy was influenced by differential outcomes in either experiment. Although the differential outcome effect has been demonstrated in many situations, it does not appear to be useful in the drug discrimination assay. Possible reasons for the lack of an observed effect are discussed. © 2002 Lippincott Williams & Wilkins.

Keywords: drug discrimination, differential outcome effect, differential outcome procedure, conditional discriminations, operant conditioning, rat

INTRODUCTION

The drug discrimination assay allows classification of stimulus effects of psychoactive drugs. One reported difficulty of this assay is the extensive time necessary to conduct a single study. The present studies sought to examine the utility of applying differential outcome procedures in two operant drug discrimination assays, in order to reduce the time required to establish stimulus control.

The differential outcomes effect (DOE) is a behavioural phenomenon in which correlating unique outcomes with individual discriminative stimuli decreases the time necessary for acquisition of a stimulus discrimination and increases the terminal accuracy of that discrimination (Goeters *et al.*, 1992). The differential outcomes procedure (DOP) refers to the actual methods employed in order to improve the terminal accuracy of a response and decrease the amount of time needed to acquire the response. Trapold (1970) described one of the first demonstrations of the DOE. He applied a DOP in a two-choice discrimination task in a standard operant chamber with rats, and demonstrated a shortened time period for acquisition of responding and better accuracy in the rats exposed to the DOP.

The usefulness of the DOP has been illustrated across many settings and subjects. For example, Jones and White (1994) used a DOP in pigeons under a delayed matching to sample procedure. Results indicated that when correct responding was correlated with differential outcomes, subjects preformed at a higher level of accuracy. Maki *et al.* (1995) reported that children taught a conditional discrimination using a DOP learned the discrimination task faster and more accurately than those who were taught using a non-differential outcomes procedure. Similar examples can be found in species ranging from domestic chickens (Poling *et al.*, 1996) to horses (Miyashita *et al.*, 2000).

The DOE has also been demonstrated across a range of stimuli and learning tasks. Urcuioli (1990) used a many-to-one matching to sample procedure, in which four sample stimuli and two comparison

stimuli were presented to pigeons. Acquisition of matching was facilitated in groups exposed to the DOP. Other task configurations that have been used with a DOP include delayed matching to sample in conditional discriminations with up to seven delay periods (Linwick *et al.*, 1988; Dube *et al.*, 1989; Alling *et al.*, 1991), successive discriminations with eight object pairs presented on any given trial (Litt and Schreiban, 1981), and even two-choice successive discriminations with avoidance components (Overmier *et al.*, 1971). Additionally, a DOE has been reported in at least one study where three response options were used (Janssen and Guess, 1978). Indeed, Goeters *et al.* (1992) reported that the DOP appears to be especially useful in more complex discriminations.

Although the literature suggests that a DOP can enhance acquisition of complex discriminations based on exteroceptive stimuli, the role that a DOP may play in discriminations based on interoceptive stimuli is unknown. The drug discrimination assay is one such procedure. In this procedure, physiological changes produced by a drug can serve as internal discriminative stimuli that signal the availability of reward. Once a discrimination is established, other psychoactive drugs are often administered to examine whether these will produce discriminative stimulus effects similar to those of the training drug, and thus provide a behavioural index of mechanisms of action. Generally, in a two-lever discrimination, a novel drug is thought to produce interoceptive stimuli similar to those of a training drug if, while under the influence of the novel drug, the subject emits at least 80% of responses on the lever appropriate to the training drug. Pharmacological specificity of this response is indicated if it can be blocked by pretreatment with another drug known to antagonize the effects of the training drug.

One important consideration when interpreting data in drug discrimination studies is that subjects will respond regardless of the stimulus properties of a particular compound. This may make results difficult to interpret if the administration of novel compounds produces between 20% and 80% drug-appropriate responding, i.e. 'partial substitution'. These results are problematic because there are no clear indications for interpretation. For example, consider a subject trained to discriminate a psychostimulant (e.g. D-amphetamine) from saline, and then administered a novel compound that results in 70% D-amphetamine responding. If that compound produces at least 80% drug-appropriate responding, one may conclude that the stimulus effects of the novel compound are similar to those of D-amphetamine. If the subject emits less than 20% of responses on the D-amphetamine lever, one may conclude the stimulus effects of the novel compound are distinctly different from those of D-amphetamine. However, with 70% drug-appropriate responding, the conclusion is unclear. In an attempt to compensate for this limitation, other drug discrimination procedures have been employed. One such method is the use of more complex discriminations, such as three-choice discriminations (Stolerman, 1993, chapter 9). The use of three discriminative stimuli provides subjects with another 'choice' during test sessions. This results in an enhanced specificity of discriminations, leaving less room for 'partial substitution'. In the example above, the percentage of responding on the D-amphetamine appropriate lever may have been quite different had the subject been trained to discriminate D-amphetamine and saline from a third compound. However, although the three-choice method is a more sensitive measure of the stimulus effects of psychoactive compounds, the increased sensitivity provided by three-choice procedures significantly prolongs the amount of time required to complete a study.

The increased time required to conduct three-choice studies is due in part to additional maintenance training sessions required under each stimulus condition between test sessions. That is, in a traditional two-choice discrimination there are two maintenance training sessions between test sessions, and the addition of a third choice increases the number of training sessions between test sessions to at least three. Additionally, the methodological constraint that novel compounds should be administered during test sessions in equal numbers following each training condition, without administering any drug for more than two consecutive days, increases the time requirement. Thus, a procedure that shortens acquisition time for discriminations and enhances terminal accuracy of responding would be an invaluable tool for drug discrimination research. Morgan and Baker (1997) demonstrated a shortened acquisition period in a cocaine–saline discrimination in rats exposed to differential outcomes. The group exposed to the DOP reached criterion for discrimination significantly faster (mean number of 34 versus 45 sessions) than the control group.

Given that the DOE has been demonstrated across several subjects and in several types of procedures using various types of stimuli, that the DOE is more pronounced when stimulus control is difficult to establish, and that preliminary results in one drug discrimination study support the notion that DOP shortens acquisition time, the present studies investigated whether application of a DOP would also improve acquisition of three-choice drug discriminations. First ('Experiment One'), a DOP was used in a

three-choice discrimination between (±)-3,4-methylenedioxymethamphetamine (MDMA), D-amphetamine and saline. Second ('Experiment Two'), a DOP was used in a three-choice discrimination between MDMA, (+)-lysergic acid diethylamide (LSD) and saline.

The two studies were designed to examine the stimulus properties of MDMA, a commonly abused drug generally known as 'ecstasy'. Currently, MDMA is classified as both a stimulant and a hallucinogen, though the mechanisms of action responsible for the stimulus effects of this substance are unclear. The more traditional two-choice discriminations using MDMA and saline have produced conflicting results. MDMA appears to produce discriminative stimulus effects similar to those of both LSD and D-amphetamine. However, the degree of similarity appears to depend on the training drug, as well as other methodological variables that differ among researchers. Though it has been reported that MDMA produced full stimulus generalization in animals trained to discriminate amphetamine from saline (Evans and Johanson, 1986; Glennon and Young, 1984), Oberlander and Nichols (1988) did not replicate these findings. When MDMA is administered in rats trained to discriminate LSD from 'another' compound (i.e. cocaine or pentobarbitone), MDMA has been reported to substitute for LSD (Appel *et al.*, 1999). However, when subjects are trained to discriminate LSD from saline, MDMA is reported not to substitute for LSD (Appel *et al.*, 1999; Callahan and Appel, 1988). Similar conflicts are reported when MDMA has been used as the training stimulus. D-Amphetamine has been reported to produce only partial stimulus generalization (Baker and Makhay, 1996; Glennon and Misenheimer, 1989; Schechter, 1987) to MDMA, and LSD has been reported to produce stimulus generalization by some researchers (Oberlander and Nichols, 1988; Schechter 1998), but not by others (Baker *et al.*, 1995). The present studies investigated: (1) if MDMA could be differentiated from a classic psychostimulant (i.e. D-amphetamine) in a three-choice assay, (2) if MDMA could be differentiated from a classic hallucinogen (i.e. LSD) in a separate three-choice assay, and (3) if the use of a DOP in either study would shorten the amount of time required to acquire the discrimination and/or facilitate terminal accuracy of these discriminations. Some of the data from Experiment One have been previously published (Goodwin and Baker, 2000), although they were not analysed for the DOE.

The experimental protocols described below were reviewed by the Institutional Animal Care and Use Committee of Western Michigan University, USA, and subjects were maintained according to the general principles of animal husbandry outlined in the *Guidelines of the Committee on Care and Use of Laboratory Animal Resources* (National Research Council, 1996).

METHODS

Subjects

Subjects consisted of 40 experimentally naïve, male Sprague–Dawley rats aged 50–60 days (Harlan Breeding Laboratories, Indianapolis, IN, USA). All rats were housed individually in colonies maintained on a 12/12 h light–dark cycle (07.00 h to 19.00 h), at a relatively constant temperature ($20 \pm 2^{\circ}$C) and humidity ($50 \pm 5\%$). Animals were allowed one week to acclimatize to the colony environment prior to the initiation of each experiment. Subjects in Experiment One ($n = 16$) had free access to standard laboratory rat chow and access to water was restricted to 15–20 min following training and testing sessions and a 24-hour period on the weekends. For subjects in Experiment Two ($n = 24$) food was restricted to maintain body weights between 85% and 90% of free feeding weights, and free access to water was available in the home cages.

Apparatus

Behavioural procedures were conducted in 16 standard three-lever operant chambers (MED Associates Inc., Georgia, VT, USA). The eight operant chambers used in Experiment One ($28 \times 21 \times 21$ cm) contained three removable levers, a liquid delivery mechanism (0.1 ml), and a 28 V house light located on the front panel above the centre lever. The eight operant chambers used in Experiment Two ($30 \times 31 \times 24$ cm) contained three automatic retractable levers, three stimulus lights located above the levers, a food pellet delivery mechanism and a 28 V house light located on the back panel. All 16 chambers were individually housed in sound- and light-attenuating cubicles with fans to provide both ventilation and masking noise.

In Experiment One, reinforcers consisted of water or different flavours of sweetened condensed milk, which was purchased commercially and diluted in the laboratory with tap water at a 3:1 ratio.

In Experiment Two, lights and tones correlated with the presentation of food pellets (Bioserv, Frenchtown, NJ, USA) were employed as the differential outcomes. The primary rationale for this change was that the use of visual and auditory stimuli rather than gustatory or odour stimuli might increase systematic generality of the findings. The modality of reward was changed to food in Experiment Two

because the operant chambers with the capacity to programme tones and lights contained a food delivery mechanism.

Experiment One

In the differential outcome group ($n = 8$), MDMA and D-amphetamine were consistently correlated with either plain sweetened condensed milk or chocolate-flavoured sweetened condensed milk as reinforcers. Lever assignments and reinforcer presentation were counterbalanced across subjects. Four of the rats always received plain sweetened condensed milk as the reinforcer when MDMA was administered and chocolate sweetened condensed milk when D-amphetamine was administered. The other four rats always received plain sweetened condensed milk when D-amphetamine was administered and chocolate sweetened condensed milk when MDMA was administered. Within the differential outcome group, four rats were reinforced for responding on one lever after administration of MDMA and the opposite lever after administration of D-amphetamine. The lever assignments were reversed for the remaining four rats. All eight rats in the differential outcome group were reinforced with water for pressing the centre lever after administration of saline.

The control group ($n = 8$) received water, plain or chocolate sweetened condensed milk as reinforcers on a non-systematic basis, and all subjects received the same reinforcer type during daily training sessions. For example, the control group received chocolate sweetened condensed milk as the reinforcer following saline administration for a given training session and then received water as the reinforcer the next day following D-amphetamine administration. Saline, MDMA and D-amphetamine were never consistently paired with any outcome for the control group. In this way, no pattern was established in which the control group could correlate any outcome with any discriminative stimulus condition. All eight rats in the control group were reinforced for responding on the centre lever when saline was administered, though the reinforcer delivered varied. Lever assignments following MDMA and D-amphetamine administration were also counterbalanced across subjects within the control group. Table 1 illustrates the reinforcer and lever assignments for both groups in Experiment One.

An autoshaping procedure was used for the first week of the experiment. Subjects received between five and six one-hour sessions in which no substances were administered, no levers were present in the chamber, and water reinforcement was delivered on a fixed-time one minute (FT 1) schedule. Following the autoshaping procedure, errorless discrimination training was employed in which only the condition-appropriate lever was present for alternate 20 min training sessions preceded by injection of saline or a drug. The order of presentation of each stimulus was the same for each subject for the twelve total errorless training sessions. The first errorless training session was preceded by saline, the next by D-amphetamine, and the next by MDMA. The fourth errorless training session was preceded by saline, the fifth by MDMA, and the last by D-amphetamine. This procedure was continued until each subject was exposed to a total of four errorless training sessions for each of the three conditions (saline, D-amphetamine or MDMA). During errorless training sessions, a fixed-ratio one minute (FR 1) schedule of reinforcement was in effect and the appropriate outcomes were presented to the differential outcome group. The control group received the three outcomes on a non-systematic basis.

Following the errorless training procedure, all three levers were presented and discrimination training began with a FR 1 schedule of reinforcement during daily 20 min training sessions. The ratio was gradually increased to 10 as responding became stable. Reinforcement was contingent on 10 consecutive responses on the condition-appropriate lever, responses on any other lever reset the response counter, and reinforcement was not delivered until 10 consecutive responses were made on the condition-appropriate lever. Subjects were able to obtain an unlimited number of reinforcers during training sessions. All levers were wiped with isopropyl alcohol between training sessions to reduce the effects of

TABLE 1. Reinforcer and lever assignments for Experiment One

No. subjects	Group	MDMA-lever	MDMA-outcome	AMPH-lever	AMPH-outcome	Saline-lever	Saline-outcome
2	control	left	variable	right	variable	centre	variable
2	control	right	variable	left	variable	centre	variable
2	DOP	left	plain milk	right	chocolate milk	centre	water
2	DOP	right	chocolate milk	left	plain milk	centre	water
2	control	left	variable	right	variable	centre	variable
2	control	right	variable	left	variable	centre	variable
2	DOP	left	chocolate milk	right	plain milk	centre	water
2	DOP	right	plain milk	left	chocolate milk	centre	water

olfactory cues in the operant chambers (Extance and Goudie, 1981).

Experiment two

The training procedures were conducted in the same manner as in Experiment One, with the following exceptions. The discriminative stimulus conditions consisted of MDMA, saline and LSD, and reinforcers consisted of food pellets. Additionally, the delivery of food pellets under the MDMA and LSD conditions were correlated with either a brief tone or two flashes of three stimulus lights located above the levers. That is, within the differential outcome group ($n = 12$), six subjects were exposed to a brief tone each time a reinforcer (i.e. food pellet) was delivered under the MDMA condition and exposed to two flashes of the stimulus lights with the delivery of reinforcement under the LSD condition. The opposite was true for the remaining six subjects in the differential outcome group. The outcome associated with the saline condition for all subjects in the differential outcome group was the delivery of food pellets only.

Subjects in the control group ($n = 12$) were exposed to the different outcomes in a similar non-systematic basis as described for Experiment One. That is, all subjects in the control group were exposed to the same outcome for any given training session, but the presentation of outcomes was never correlated with a particular drug or saline. In this way, no pattern could be established where the administration of either saline, LSD or MDMA would reliably signal what outcome would be presented. Table 2 illustrates outcome and lever assignments for Experiment Two.

Drugs

D-Amphetamine sulphate (1.0 mg/kg), (±)-3,4-methylenedioxymethamphetamine (MDMA) hydrochloride (1.5 mg/kg), and (+)-lysergic acid diethylamide (LSD) (0.08 mg/kg), were obtained from the National Institutes on Drug Abuse (Rockville, MD, USA). Drug doses were chosen based on previous studies in this laboratory and a review of doses used in other published studies. In both experiments, injections were administered i.p. 15 min prior to training or testing sessions. Aseptic injection techniques and sterile 1 cm^3 tuberculin syringes were utilized. Drug solutions were prepared in sterile bacteriostatic saline (0.90%) and injected in a volume of 1 ml/kg.

Data analyses

For Experiment One, the criterion for acquisition of the discrimination was 80–100% stimulus-appropriate responding prior to the delivery of the first reinforcer for eight out of ten consecutive training sessions. The numbering of training sessions began once subjects reached the terminal FR 10. The difference between groups was compared using a *t*-test. Terminal accuracy was analysed between groups using linear regression analysis. Terminal accuracy was defined as the percentage of stimulus-appropriate responding prior to the delivery of reinforcement during each training session. Group averages of terminal accuracy were determined and plotted for 100 sessions, beginning with the session at which subjects were reliably responding on the FR 10 schedule.

The same acquisition criterion was used in Experiment Two. However, once the discrimination criterion was initially met, results of stimulus generalization tests with the training drugs indicated that several of the subjects exhibited poor stimulus control. Although the operant chambers were wiped with isopropyl alcohol between sessions, it is possible subjects were relying on olfactory cues during training sessions. Therefore, instead of continuing to administer the same training stimulus to all 24 subjects, the three stimulus conditions were varied so that subjects that were run in the same chambers received a different training stimulus each day. In this way, any remaining olfactory cues were not reliable prompts for identification of the lever producing reinforcement during that session. Following this change, subjects were again required to meet the criterion for discrimination (80–100% stimulus-appropriate responding prior to the delivery of the first reinforcer for eight out of 10 consecutive training

TABLE 2. Outcome and lever assignments for Experiment Two

No. subjects	Group	MDMA-lever	MDMA-outcome	AMPH-lever	AMPH-outcome	Saline-lever	Saline-outcome
3	DOP	left	light	right	tone	centre	absence of tone/light
3	DOP	right	tone	left	light	centre	absence of tone/light
3	DOP	left	light	right	tone	centre	absence of tone/light
3	DOP	right	tone	left	light	centre	absence of tone/light
3	control	left	variable	right	variable	centre	variable
3	control	right	variable	left	variable	centre	variable
3	control	left	variable	right	variable	centre	variable
3	control	right	variable	left	variable	centre	variable

sessions). The numbers of sessions to criterion, both before and after this change, were analysed using a *t*-test. Terminal accuracy was analysed and plotted as in Experiment One.

RESULTS

All 16 subjects in Experiment One acquired the discrimination of D-amphetamine and MDMA. Differential outcomes did not facilitate acquisition of the discrimination, as the number of sessions to criterion did not differ between the two groups ($t = 0.19$; NS). The control group met the discrimination criterion in an average of 66 ± 7 training sessions and the differential outcome group in an average of 68 ± 6 training sessions. Terminal accuracy, defined as the percent stimulus-appropriate responding prior to delivery of the first reinforcer, also did not differ between groups [$F(1,196) = 0.002$; NS] (Figure 1).

All 24 subjects in Experiment Two met the discrimination criterion. An analysis of the data revealed that the differential outcome procedure did not facilitate acquisition ($t = 1.15$; NS). The mean number of sessions to criterion was 55 ± 5 for the control group and 49 ± 3 for the differential outcome group. Upon presentation of different stimuli across groups, all subjects were required to again meet the discrimination criterion. The number of sessions to meet criterion the second time was also not significantly different between the differential outcome and control groups ($t = 0.27$; NS). The mean number of *total* training sessions to meet the criterion was 153 ± 2.9 for the control group and 159 ± 5.1 for the differential outcome group. Figure 2 illustrates the terminal accuracy for the first 100 training sessions of Experiment Two. The training sessions were again numbered following achievement of the terminal FR 10. A linear regression analysis illustrated there was no difference between the differential outcome and control groups [$F(1,194) = 0.29$; NS].

DISCUSSION

The drug discrimination assay can provide behavioural information about neurochemical changes associated with the administration of psychoactive drugs in living organisms. The assay measures aspects of subjective effects of compounds by requiring subjects to perform a specific behaviour in the presence of one drug and a different behaviour in the presence of another compound. Comparisons of behaviour evoked by novel compounds to that evoked by a standard psychoactive drug with a known mechanism of action can provide information about the similarity of the novel drug and the standard. Such information has made major contributions to development of pharmacological treatments for substance abuse. Unfortunately, the amount of time required to conduct drug discrimination studies, especially those involving complex discriminations, is a limitation of such research.

Previous studies of the acquisition of discriminative control by exteroceptive stimuli suggest that DOPs can yield both an increase in terminal accuracy of responses and decreased acquisition time. The usefulness of the procedure in assays that employ interoceptive stimuli is relatively unknown. Morgan and Baker (1997) demonstrated a shortened acquisition period in a two-choice cocaine versus saline discrimination. Although the DOE is reported to be greater with more complex discriminations (Goeters *et al.*, 1992), the results of the present studies did not demonstrate any difference in acquisition time or terminal accuracy in two complex drug discrimination procedures in which DOPs were used.

Experiment One sought to examine the effects of a DOP on responding in a discrimination task where different flavours of sweetened milk and water served as the differential outcomes for reinforced behaviours. The lack of any improved acquisition of discrimination may have arisen from development of a preference for one or the other outcome. That is,

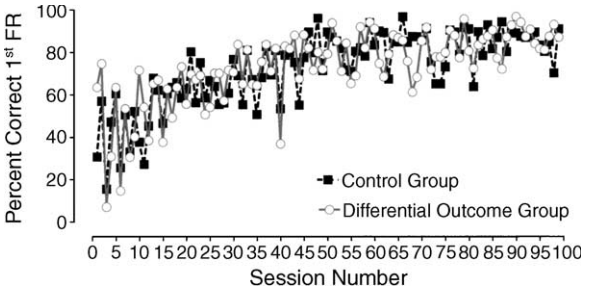

FIGURE 1. Terminal accuracy for 100 sessions of Experiment One (see text), calculated as daily group means of the percent correct for the first FR ($n = 8$ for each group).

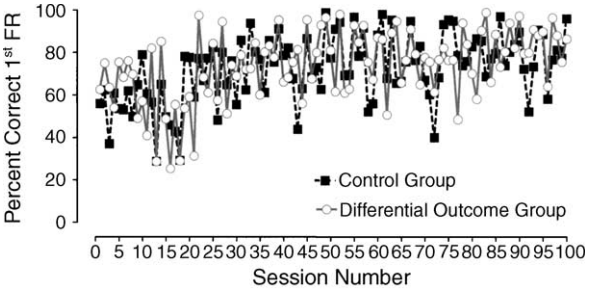

FIGURE 2. Terminal accuracy for 100 sessions of Experiment 2 (see text), calculated as daily group means of the percent correct for the first FR ($n = 12$ for each group).

the different flavours of sweetened condensed milk and water were not necessarily *equivalent* reinforcers. The development of a preference for one outcome (e.g. chocolate sweetened condensed milk) over the others (e.g. plain sweetened condensed milk or water) could mask the effects of the actual differential outcome procedure. However, the DOE has been reported in studies that employed outcomes that might be expected to generate differences in preference. For example, Urcuioli (1991) used the presentation of food versus the presentation of a light as outcomes in a two-choice conditional matching-to-sample discrimination in pigeons and reported a DOE. Additionally, Fedorchak *et al.* (1986) observed a DOE in rats using a two-choice successive discrimination with water or water paired with a light as the outcomes.

In order to eliminate possible differences in reinforcer preference that may have resulted in the absence of a DOE in Experiment One, and to investigate more fully the potential utility of the DOP in acquisition of interoceptive discriminations, we implemented non-appetitive outcomes in Experiment Two. Computer generated outcomes (i.e. lights and tones) were correlated with the presentation of food reinforcement. This could potentially alter the results in two ways. First, using neutral outcomes (e.g. a light or a tone) paired with the same reinforcer (e.g. a food pellet) for all conditions may remove the possible effect of a preference for one of the outcomes. Second, the presentation of the outcomes would be precise and the influence of potential human error when diluting the milk would be eliminated. Unfortunately, our results indicate this DOP was also unsuccessful in decreasing the time required to acquire a complex drug discrimination.

Nearly all studies using a differential outcome procedure have employed external cues as the discriminative stimuli. The drug discrimination assay is unique in that it establishes drug states as internal discriminative stimuli. Unlike conditional discriminations with external cues, it would be difficult to present more than one drug state as a stimulus during a single training session. It is not possible to induce a drug state, then remove it and replace the cue with vehicle or another drug state within a single session, without using highly selective agonists and antagonists, which may conceivably add extraneous variables. The inability to present multiple stimuli within one session may account for the lack of an effect of the DOPs used in these two complex drug discriminations.

Contrary to the present findings, Morgan and Baker (1997) reported a DOP significantly shortened the time required to establish a cocaine–saline discrimination. However, although the difference was statistically significant, it may not be practically significant when considered together with the actual number of sessions required to establish the discrimination. The differential outcome group required a mean of 34 sessions and the control group required a mean of 45 sessions. Essentially, the DOP shortened acquisition by fewer than 15 sessions in an assay where a total of over 125 sessions is common. The difference in the number of sessions to criterion may need to be more than *statistically* significant in order for a DOP to serve as a tool in drug discrimination research.

It is worth mentioning that there are other methods used in drug discrimination research that appear to result in faster acquisition than the operant lever method. The T-maze was one of the first methods used to study the discriminative stimulus properties of drugs and is reported to require short periods of acquisition (Overton, 1991). However, although the T-maze appears to require short periods of acquisition, it has also been reported to be less sensitive to drug effects and to require considerably larger doses of drugs to establish and maintain stimulus control than those required in the operant lever method (Stolerman, 1993). The conditioned taste aversion assay has also been shown to require fewer training sessions to establish stimulus control than the operant lever method (Stolerman, 1993). Although these procedures appear to produce acquisition of stimulus control more rapidly than standard operant conditioning techniques, the conditioned taste aversion design is essentially equal to a one-lever operant task because the subjects can either drink the solution or not; there is no second option. It is well-documented that the one-lever operant task is less sensitive to drug effects than are the two- and three-lever designs (Stolerman, 1993).

In conclusion, the stimulus effects of MDMA are distinguishable from those of D-amphetamine and LSD, and application of a DOP was not effective in reducing the amount of time needed to acquire either discrimination nor did it facilitate terminal accuracy. Thus, it is clear that although the DOE is a documented behavioural phenomenon, it does not have practical utility in the drug discrimination assay.

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