*PREFERENCE IN RHESUS MONKEYS GIVEN A CHOICE
BETWEEN COCAINE AND d,l-CATHINONE*

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Previous experiments have shown that both cocaine and *d,l*-cathinone can function as positive reinforcers when delivered intravenously to rhesus monkeys. However, the relative reinforcing efficacies of these compounds have not been established. In the present experiment, three rhesus monkeys were allowed to choose between saline and several doses of *d,l*-cathinone or cocaine as well as between several doses of both drugs in a discrete-trial choice procedure. Sufficient doses (.05 to .2 mg/kg/injection) of either drug maintained self-administration and the higher doses were reliably preferred to saline. Doses of *d,l*-cathinone that were preferred to saline were then compared to a range of cocaine doses in drug-drug choice. As the dose of *d,l*-cathinone that was available was increased, an increase in cocaine dose was necessary to maintain cocaine preference. Comparison of drug-drug choice data to dose combinations predicted to be chosen with equal frequency revealed that the reinforcing efficacy of *d,l*-cathinone was equivalent to that of cocaine.

Key words: choice, cathinone, cocaine, reinforcing efficacy, self-administration, lever press, rhesus monkey

Khat (*Catha edulis*) is a shrub which is found in certain areas of East Africa and the Arabian peninsula. The leaves of the plant are chewed by natives of this area, apparently for their psychomotor stimulant effects. Cathinone is the alkaloid of the khat plant that is primarily responsible for these effects (Halbach, 1972; Knoll, 1980). Laboratory investigations of the behavioral and neurochemical effects of both *l*- and *d,l*-cathinone have shown their actions to be essentially amphetamine-like. Both compounds increase locomotor activity, induce stereotyped behavior, and decrease food intake (Kalix, 1980a, 1980b; Zelger & Carlini, 1980), and cross-tolerance develops between the effects of *d*-amphetamine and *d,l*-cathinone on

milk intake in rats (Foltin & Schuster, 1982). Each has been shown to produce amphetamine-like effects on operant behavior and to function as a positive reinforcer when delivered intravenously to rhesus monkeys under a fixed-ratio (FR) 10 schedule (Johanson & Schuster, 1981). Moreover, in rats trained to discriminate *d*-amphetamine from saline in a drug discrimination paradigm, *d,l*-cathinone resulted in *d*-amphetamine-appropriate responding (Rosecrans, Campbell, Dewey, & Harris, 1980). Neurochemically, *d*-amphetamine and *d,l*- and *l*-cathinone enhance dopamine synaptic transmission in rodent brain (Kalix, 1981; Rosecrans et al., 1980; Wagner, Preston, Ricaurte, Schuster, & Seiden 1982; Zelger & Carlini, 1981). *d*-Amphetamine and *l*-cathinone have also been shown to be indistinguishable in terms of their cardiovascular effects (Kohli & Goldberg, 1982). Based on these experiments, the principal difference between cathinone and *d*-amphetamine appears to be one of duration of action, cathinone being the shorter acting of the two.

In the self-administration study by Johanson and Schuster (1981), *d,l*-cathinone consistently maintained higher rates of responding across a wider range of doses than did *d*-amphet-

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amine under a FR 10 schedule of drug injection. From these data, it would be tempting to conclude that *d,l*-cathinone is a "stronger" or "better" positive reinforcer than *d*-amphetamine. However, the rate of responding for a drug under these conditions is determined not only by its reinforcing properties but also by its direct rate-modifying effects and duration of action (see Johanson, 1978). For a more direct quantification of the reinforcing properties of a drug it is desirable to use a method that directly measures the effectiveness of the drug as a reinforcer relative to other reinforcing stimuli while minimizing the influence of other effects. As with other reinforcing stimuli, discrete-trial choice procedures (Griffiths, Wurster, & Brady, 1975, 1981; Johanson & Schuster, 1975, 1977; Woolverton & Balster, 1981), concurrent-access procedures (Iglauer & Woods, 1974; Llewellyn, Iglauer, & Woods, 1976) and progressive-ratio procedures (Griffiths, Brady, & Snell, 1978; Yanagita, 1973) have all been used to evaluate drugs as reinforcers. Each method allows a quantitative estimate of the reinforcing properties of a drug by providing a measure of the strength of the behavior that leads to its delivery (Skinner, 1938). A consistent finding of this research has been that a higher drug dose maintains a greater frequency of choice in a discrete-trial choice procedure, a greater proportion of responding under conditions of concurrent access, or a greater total number of responses in a progressive-ratio procedure than does a lower drug dose. Thus, as has been found with other reinforcing stimuli, an increase in reinforcement magnitude often decreases response rate under simple schedules of reinforcement but increases the strength of the behavior that leads to its delivery (Brownstein, 1971; Catania, 1963; Hodos & Kalman, 1963). It has been assumed that this increase in response strength reflects enhanced strength as a reinforcer. The term that has been used in the self-administration literature to refer to this property of a drug is *reinforcing efficacy* (Johanson & Schuster, 1977; Schuster, 1975).

Although, *d,l*-cathinone can function as a positive reinforcer, its efficacy relative to other positive reinforcers has not been established. The present experiment was designed to estimate the reinforcing efficacy of *d,l*-cathinone relative to another drug reinforcer, cocaine, using a discrete-trial choice procedure. Mon-

keys were allowed to choose between an intravenous injection of *d,l*-cathinone or cocaine every 5 or 15 min for several hours each day. The results indicate that *d,l*-cathinone can function as a positive reinforcer in a discrete-trial choice procedure and has reinforcing efficacy that is equivalent to that of cocaine.

METHOD

The method used was a switching choice procedure similar to that used by several other investigators (Aigner & Balster, 1978; Findley, Robinson, & Peregrino, 1972; Griffiths et al., 1975; Johanson & Aigner, 1981; Woolverton & Balster, 1981).

Subjects

One female (9076) and two male (8003, 6019) adult rhesus monkeys (*Macaca mulatta*) were used as subjects. The initial body weights of these animals were: 8003, 6.8 kg; 6019, 7.4 kg; 9076, 5.0 kg. Monkeys 6019 and 9076 were experimentally naive at the beginning of the experiment; Monkey 8003 had been used in an experiment involving daily self-administration of cocaine. All animals had continuous access to water and were fed 100 to 150 g of Purina Monkey Chow daily, after experimental sessions. In addition, a multi-vitamin supplement (Plex-Sol C, Vet-A-Mix, Inc.) was dissolved in the water and fresh fruit was occasionally provided.

Each animal was surgically prepared with an intravenous polyvinyl chloride double-lumen catheter (U.S. Catheter and Instrument Company) under sodium pentobarbital anesthesia (up to 30 mg/kg, iv, as needed). The proximal end of the catheter was inserted into a major vein and terminated near the superior vena cava; the distal end was threaded subcutaneously and exited through an incision in the back of the animal. The use of the double-lumen catheter allowed the sequential delivery of two drug solutions without intermixing.

Apparatus

Each animal was housed throughout the experiment in a wooden, front-opening, sound-attenuating chamber that was 68.6 cm wide, 76.2 cm high, and 83.8 cm deep. A fan was located on the front door for ventilation. The monkeys were visually isolated but a wide-angle lens allowed observation of the monkey.

On the inside of the front door were two metal boxes (15.2 by 12.7 by 10.2 cm), 20 cm from the floor and 10 cm from the center, each containing a response lever (BRS/LVE, PRL-001) and four stimulus lights (0.028 W). On the left lever (Lever 1) the lights were covered with white Dialco lens caps and on the right lever (Lever 2) two lights were covered with red Dialco lens caps and two with green Dialco lens caps. The lights were 6.4 cm above the lever and evenly spaced 3.8 cm apart. In addition each chamber could be illuminated by either a white (40-W) or red (15-W) houselight located in the ceiling.

Each monkey wore a stainless steel harness that was attached to a spring arm that was 46 cm in length and 1.3 cm in diameter (E and H Engineering), which in turn was attached to the back wall of the cubicle. This arrangement allowed the monkey relatively unrestricted movement within the cubicle and provided protection for the catheter, which was threaded through the spring arm. Outside the cubicle each lumen of the catheter was connected to a separate peristaltic infusion pump (7540X, Cole-Parmer Instrument Co.), which delivered solutions at the rate of 6 ml/min.

Procedure

Each experimental session consisted of either 50 (6019) or 32 (8003, 9076) trials. At the beginning of each trial the white houselight and all Lever 1 lights were illuminated and either the red or green lights above Lever 2 were illuminated. Five consecutive responses (FR 5) on Lever 1 (switching lever) produced a stimulus change above Lever 2 (drug delivery lever); that is, if the lights above Lever 2 were red, they changed to green after each FR 5 and vice versa. At least three such stimulus changes (i.e., a sequence of three completed ratios on Lever 1) were required before drug became available contingent upon responding on Lever 2. Lever 2 responses occurring prior to the completion of these three stimulus changes reset the requirement so that three additional stimulus changes had to be completed by responding on Lever 1. Although a minimum of three switches was necessary, there were no restrictions on the maximum number of stimulus change allowed—that is, the monkey could continue responding on the switching lever and each completed FR 5 resulted in a stimulus change above Lever 2.

The first response on Lever 2 after the three-switch minimum had been completed extinguished the lights above Lever 1 and the white houselight. Responses on Lever 1 had no further consequences during the trial; that is, no additional stimulus changes could occur and the choice was “locked in.” An additional 29 responses (FR 30) on Lever 2 within 2 min (limited hold 2 min) resulted in an infusion of drug over a 10-s period (a complete trial). During this time, the lights which had been on above Lever 2 began flashing (on-off cycle of approximately 1 s). These lights continued flashing during a 5-min timeout period following drug delivery. If the monkey failed to complete the ratio requirement for drug delivery within the limited hold 2 min, all lights were extinguished for 5 min (5-min blackout) during which neither lever was operative (an incomplete trial). After either the timeout or blackout period, a new trial began. When this new trial began, the color of the lights above Lever 2 was the same as it had been when the last trial terminated. Therefore, in order for a monkey to continue choosing the same drug on successive trials, a minimum of four switches was required. A session terminated when all trials had been presented or 6 hr had elapsed, whichever occurred first. Sessions were conducted 7 days a week at the same time each day.

During each trial, one of two drug solutions (Drug 1 and Drug 2) was delivered following the completion of the FR 30 on Lever 2. The drug delivered depended upon which stimulus light (red or green) was selected by the monkey; one light color was associated with Drug 1 and the other color was associated with Drug 2. Therefore, the monkey chose one drug over the other by its choice of which stimulus light was illuminated when the first correct Lever 2 response was made.

Initially, dose-response relationships were determined for both cocaine and *d,l*-cathinone with saline as the alternative. Subsequently, animals were allowed to choose between doses of each drug presented in pairs. Combinations of doses were usually tested for 6 to 10 sessions, although up to 14 sessions were occasionally necessary when a trend was noted in the data. If one drug was chosen on more than 75% of the completed trials for three consecutive sessions, one of two manipulations was undertaken. If the stimulus color that had been

chosen in the last comparison in which a preference was observed was still being chosen, the light stimuli were reversed with no dose change so that the animal had to reverse its color selection in order to continue self-administering the preferred solution. If, on the other hand, a new stimulus light was being chosen, a dose change was made that was predicted to alter the color chosen (light stimuli were not changed). If the animal failed to choose the other color light following either of these manipulations, the other manipulation was undertaken. In this way it was possible to assure that the preferences observed were drug preferences rather than color preferences. If less than 75% choice frequency was seen and no trends were apparent after 10 sessions, the dose of one of the drugs was changed.

Data Analyses. During each session, the following data were recorded: trials completed with Drug 1 and Drug 2, completed switches, incorrect Lever 2 responses, incomplete trials (limited hold exceeded) in the presence of each Lever 2 stimulus, and the elapsed time between the first and 30th response of each ratio completed on Lever 2 in the presence of each stimulus. All data analyses are based upon performance during the last three sessions of each comparison. Choice results are expressed in terms of the mean percentage of completed trials in which cocaine was selected. The mean and range of values are presented for individual animals and the mean and standard error of these values are presented for the group. Rates of responding on Lever 2 (running rate between the first and last response) for each drug were also compared. Dose-response data for percentage choice were analyzed by the method of least squares linear regression (Brownlee, 1965). This analysis allowed the calculation of doses that would be predicted to engender a given choice frequency. For example, the ED_{70} is that dose predicted to result in 70% choice frequency.

Drug Solutions. Cocaine hydrochloride (National Institute on Drug Abuse) and *d,l*-cathinone hydrochloride (United Nations Narcotics Laboratory) were each dissolved in .9% saline for use in this experiment. Fresh cocaine solutions were prepared at least once a week. Because of the reported instability of the cathinone (Braenden, 1980), *d,l*-cathinone solutions were prepared before every other session. Concentrations were appropriate for an injection

volume of approximately 1.0 ml. All doses are expressed in terms of the salt.

RESULTS

Stable performance by each monkey developed under .1 mg/kg/injection cocaine versus saline conditions within approximately 60 experimental sessions. When light stimuli were reversed under these conditions, each animal reversed its color choice within 10 sessions.

The results of the choice comparisons for individual animals, as well as the average for the group, are shown in Figure 1. When animals were given a choice between either cocaine and saline or *d,l*-cathinone and saline, the frequency of drug choice was dose-related. The range of doses over which choice frequency increased from 50% (no preference) to approximately 100% was similar for each drug (.05 to .2 mg/kg/injection). Linearity was acceptable for all dose-response functions ($p < .05$). For the group, the ED_{50} for cocaine in this comparison was .026 mg/kg/injection (.016 to .036, 95% confidence limits); the ED_{50} for *d,l*-cathinone was .032 mg/kg/injection (.007 to .051, 95% confidence limits). When *d,l*-cathinone was the alternative to cocaine, cocaine choice was still dose-related. However, as the dose of *d,l*-cathinone was increased, higher doses of cocaine were necessary to produce a cocaine preference. This is evidenced by a shift to the right and down in the cocaine dose-response function with successively higher doses of *d,l*-cathinone (Figure 1).

Assessment of choice performance of individual animals revealed two different patterns of behavior (Table 1). All animals locked in all available choices. However, under conditions in which 75% or greater choice frequency was observed, Monkeys 8003 and 9076 locked in the same number of trials for each alternative but usually failed to complete the FR 30 requirement for the nonpreferred choice within the period of the limited hold. Under conditions in which no preference was seen, each alternative was completed with approximately equal frequency. On the other hand, Monkey 6019 completed virtually all choice trials he locked in. Although the mean percentage completed trials for 6019 for the nonpreferred option was 73%, this was the result of averaging one comparison in which not one of the nonpreferred trials was completed with

Fig. 1. Cocaine and *d,l*-cathinone choice results for the three individual monkeys and the group mean. The percentage of completed trials (out of 32 or 50 available) on which cocaine was chosen is plotted as a function of cocaine dose and *d,l*-cathinone dose. Cocaine doses are on the abscissae and *d,l*-cathinone doses are represented by the following symbols: (●), saline; (△), .05 mg/kg/injection; (■), .1 mg/kg/injection; (▲), .2 mg/kg/injection. Each point is the mean of the last three sessions under each condition. For individual animals, vertical lines are the range of these values. For the group, vertical lines are the standard error of the mean. Occasionally variability was smaller than the symbol.

three comparisons in which greater than 90% of the nonpreferred trials were completed.

Comparisons of running rates for individual animals revealed that rate was poorly correlated with preference. In 22% (4/18) of the comparisons in which 75% or greater choice frequency was observed, the rate of responding for the preferred option was higher than that for the nonpreferred option. In 78% of the cases the ranges of the rates for preferred and nonpreferred option overlapped. In 92%

(12/13) of the cases in which no preference was seen, the ranges also overlapped.

These choice results established that *d,l*-cathinone, in sufficient doses, could compete effectively with cocaine as a positive reinforcer. A more precise assessment of the relative reinforcing efficacies of these two compounds was undertaken by an analysis of the data that allowed comparison of the choice results to a model predictive of doses with equal reinforcing efficacy. Dose-response lines for percentage

Table 1
Patterns of Choice Behavior in Individual Monkeys

Monkey	Trials		Preference Observed*		No Preference Observed*	
	Available	"Locked In"	Preferred Option	Nonpreferred Option	Cocaine	d,l-Cathinone
8033	32	32	92 (77-100)	45 (34- 70)	89 (66-100)	86 (80-100)
9076	32	32	93 (70-100)	32 (6- 65)	94 (89-100)	78 (37- 96)
6019	50	50	95 (84-100)	73 (0-100)	100	100 (98-100)

*These numbers represent the mean (range) of the percentage of "locked in" trials that were completed for each option in choice trials. Preference is defined as $\geq 75\%$ choice frequency for one or the other option. These data include choice comparisons when saline was the alternative.

choice were calculated for each drug when saline was the alternative, and for cocaine when .1 or .2 mg/kg/injection *d,l*-cathinone was the alternative. Data were combined for all animals at each dose and a best fit line was calculated by the method of least squares linear regression using the linear portion of each dose-response relationship. From these lines, doses (and 95% confidence limits) predicted to result in a given frequency of drug choices (ED_{50} , ED_{60} , ED_{70} , ED_{80} , and ED_{90}) were calculated for each drug when saline was the alternative. For example, the ED_{70} of cocaine versus saline was that dose that would be predicted to result in 70% cocaine choices when saline was the alternative. Pairs of functionally equivalent doses of each drug represent dose combinations that would be predicted to result in a 50% choice frequency if cocaine and *d,l*-cathinone were equally efficacious. Under these conditions, if the ED_{70} of cocaine were compared to the ED_{70} of *d,l*-cathinone, a 50% choice frequency would be predicted.

Given these predicted dose combinations, actual drug-drug choice data were analyzed in the same manner as the drug-saline data. From group data, percentage cocaine choice as a function of cocaine dose was calculated for each dose of *d,l*-cathinone (■, ▲: Figure 1, lower right). From these lines, the ED_{50} of cocaine was calculated for each dose of *d,l*-cathinone that was tested. This dose of cocaine would be predicted to be chosen as frequently as the given dose of *d,l*-cathinone (i.e., 50% choice frequency). The extent to which these empirically determined doses differed from the dose combinations predicted to have equal reinforcing efficacy represents the extent to which the drugs differed in their reinforcing efficacies.

The comparison of the results of drug-drug choice testing to those predicted from the drug-saline choice tests is shown in Figure 2. The solid line with enclosed area around it represents the dose combinations (ED_{50} , ED_{60} , ED_{70} , ED_{80} , ED_{90}) with 95% confidence limits that would be predicted to produce a 50% choice level, based upon a prediction from choice comparisons with saline as previously described. At doses of *d,l*-cathinone that were preferred to saline (.1 and .2 mg/kg/injection), comparisons between the experimental results and these predictive models were possible.

Fig. 2. Comparison of choice data with cocaine and *d,l*-cathinone to dose combinations predicted to be equally efficacious. Ordinate: dose of cocaine; abscissa: dose of *d,l*-cathinone. The solid line and circles represent dose combinations (ED_{50} , ED_{60} , ED_{70} , ED_{80} , ED_{90} , left to right) that would be predicted from drug-saline choice data to be chosen with equal frequency if cocaine and *d,l*-cathinone were equally efficacious as reinforcers in this procedure. The enclosed area represents the 95% confidence limits for each of these points. Square symbols (■) represent doses of cocaine which would be predicted to be chosen as frequently as .1 and .2 mg/kg/injection *d,l*-cathinone, based on drug-drug choice data.

When cocaine was compared to .1 mg/kg/injection *d,l*-cathinone, the ED_{50} for cocaine was within the limits of the prediction. With .2 mg/kg/injection *d,l*-cathinone, the ED_{50} of cocaine was lower than that predicted by the model but the 95% confidence limits overlapped.

DISCUSSION

The results of self-administration experiments in monkeys have proven to be extraordinarily well correlated with our knowledge of drug self-administration in humans (Johanson & Schuster, 1981; Thompson & Unna, 1977). With few exceptions, drugs that function as positive reinforcers in monkeys are those that are self-administered by humans (Griffiths & Balster, 1979; Johanson & Balster, 1978). Further, the similarities between animal and human drug self-administration patterns are striking (Griffiths, Bigelow, & Henningfield, 1980). It has previously been demonstrated that *l*-cathinone and *d,l*-cathinone can function as positive reinforcers in rhesus monkeys (Johanson & Schuster, 1981), a finding

that is consistent with the notion that cathinone plays an important role in maintaining khat chewing. The present study supports those findings and demonstrates that d,l-cathinone can function as a positive reinforcer when an alternative positive reinforcer is available. In addition, our results with a discrete-trial choice procedure suggest that d,l-cathinone is a highly efficacious positive reinforcer. These results, considered together with those of Johanson and Schuster (1981), suggest that d,l-cathinone would be self-administered by humans and that its reinforcing efficacy is similar to that of cocaine. In most experimental situations, cocaine has been found to have high reinforcing efficacy. In progressive-ratio procedures, for example, cocaine consistently maintains the highest breaking point among psychomotor stimulants (Griffiths et al., 1978). In addition, in discrete-trial choice procedures, cocaine is usually preferred to other psychomotor stimulants (Johanson & Schuster, 1975, 1977). In one experiment, when cocaine was the alternative to food in a discrete-trial choice procedure for 24 hr/day, the monkeys chose cocaine almost exclusively (Aigner & Balster, 1978). Cocaine access had to be terminated to prevent death of the animals by starvation. It seems apparent that the ability to compete with cocaine in a choice situation indicates considerable reinforcing efficacy.

It should be noted that running rate was poorly correlated with drug preference. Although this is consistent with previous findings (Johanson & Aigner, 1981), these rate calculations did not include rates of responding during uncompleted trials. In animals which locked in trials on a random basis and completed trials only for the preferred drug, the rate of responding for the nonpreferred drug was undoubtedly quite low. However, since the number of responses during incomplete trials was not recorded, precise calculation of this rate was impossible. Thus, although running rates may be poorly correlated with choice, overall response rate in this procedure may directly reflect drug preference. This is in contrast to what has been found under simple schedules of drug delivery in which overall response rate is usually inversely related to dose (Johanson, 1978).

The results of the present experiment have important implications for choice behavior in general and drug choice in particular. Al-

though a variety of stimuli can maintain similar rates and patterns of responding under simple schedules of reinforcement, differences between these stimuli become apparent when more than one is made simultaneously available to the organism (Herrnstein, 1961). The majority of experiments have involved comparisons of the same reinforcer presented either with different frequencies or in different quantities. The most general finding has been that greater frequencies or larger quantities of a reinforcer maintain a greater proportion of responding (see de Villiers, 1977). When different magnitudes of the same reinforcer or different reinforcers are made available under identical schedule conditions, maintenance of a greater proportion of responding has been assumed to reflect some property of a reinforcing event variously termed "reward strength" or "value" (Hodos & Valenstein, 1962; Neuringer, 1967). In the case of psychoactive drugs, the term *reinforcing efficacy* has been used to describe this property, so as to be consistent with the pharmacological concept of efficacy (Gilman, Mayer, & Melmon, 1980; Johanson & Schuster, 1975; Schuster, 1975). A drug or dose of drug that maintains a larger proportion of responding than another in a choice situation is assumed to have greater reinforcing efficacy. It is evident that drug self-administration in a choice situation is consistent with what is known about choice behavior using other positive reinforcers (Findley et al., 1972; Griffiths et al., 1975; Johanson & Schuster, 1975; Woolverton & Balster, 1981). Frequency of drug choice is directly related to drug dose (reinforcement magnitude) and can be altered by manipulating the magnitude of the alternative.

An estimate of the relative reinforcing efficacy of a drug is of value for several reasons. Quantification of efficacy allows an evaluation of behavioral and pharmacological variables that may modify it (Griffiths et al., 1975; Johanson, 1977; Woolverton & Balster, 1981). Furthermore, such estimates are essential to decisions regarding legal restrictions on drug availability. However, only a limited amount of research has been done in this regard. An important question to ask is whether efficacy in one context is predictive of efficacy in another. This is equivalent to asking whether drug choice is transitive (Sidman & Tailby, 1982). One implication of transitivity that it

is possible to evaluate in the present experiment is whether doses of two drugs that were chosen with equal frequency relative to saline were chosen with equal frequency in drug-drug choice comparisons. The analysis in Figure 2 assesses this possibility. The extent to which the experimentally determined points fall outside the enclosed area in Figure 2 represents the extent to which transitivity does not hold. Although there is a tendency to deviate from transitivity at high doses of cocaine, the difference is not statistically significant. It is interesting, however, to speculate upon the interpretation of a lack of transitivity in the data. If the experimental data points fell below the enclosed area in Figure 2, it could be concluded that cocaine was a more efficacious positive reinforcer than *d,l*-cathinone. That is, deviation from transitivity may be a definition of differences in the relative reinforcing efficacies of two compounds. Although choice results with saline as the alternative to drug demonstrate the efficacy of a drug in this procedure, direct drug-drug choice comparisons may be necessary to establish differences in relative reinforcing efficacy.

In summary, *d,l*-cathinone was able to function as a positive reinforcer in a discrete-trial choice procedure and, in drug-drug choice comparisons, *d,l*-cathinone and cocaine were equally efficacious. Although variables such as the schedule of drug delivery can alter the functional properties of stimuli, including drugs (Goldberg & Spealman, 1982; Kelleher & Morse, 1968; Spealman, 1979), under the present conditions these factors are presumed to be equivalent for the two drugs. Thus, the data suggest that *d,l*-cathinone is a highly efficacious positive reinforcer. Under conditions in which the response cost for cocaine was high, *d,l*-cathinone might be predicted to become a highly preferred positive reinforcer. Deviation of drug-drug choice behavior from transitivity may be necessary for the demonstration of differences in the relative reinforcing efficacies of drugs in a choice paradigm.

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