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Cocaine Reinforced Progressive Ratio Performance in the Rhesus Monkey[1,2,3]

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BEDFORD, J. A., L. P. BAILEY AND M. C. WILSON. *Cocaine reinforced progressive ratio performance in the rhesus monkey*. PHARMAC. BIOCHEM. BEHAV. 9(5) 631–638, 1978.—A series of experiments were conducted to determine the effectiveness of a progressive ratio (PR) procedure in measuring the relative reinforcing efficacy of several intravenous doses of cocaine. In Experiment 1, utilizing much smaller increases in the ratio requirement than previously reported, the animals generally displayed increases in breaking point with increases in the cocaine unit dose up to 0.4 mg/kg/inj. The highest dose studied (0.8 mg/kg/inj.) engendered breaking points lower than the 0.4 mg/kg dose but higher than the remaining lower doses. Experiment 2 was conducted utilizing the same reinforcement schedule as in Experiment 1 but with liquid Tang® as the reward. The results demonstrated that this procedure would function to discriminate reinforcing strength with a more traditional reward. Experiment 3 examined a more expedient procedure to see if results similar to those seen in Experiment 1 could be obtained in a shorter period of time. However, the shorter procedure engendered excessive intrasubject variability, suggesting that some intermediate level of baseline experience between the 5–7 days used in Experiment 1 and the 50 reinforced responses used in Experiment 3 would be necessary to obtain consistent breaking point-unit dose functions.

Cocaine Progressive ratio Rhesus monkey Self administration Reinforcing efficacy Abuse potential

THE PROGRESSIVE ratio procedure has been reported to be an effective procedure for measuring the relative reinforcing strength of several traditional reinforcers. Basically the procedure involves increasing the ratio requirement (i.e., response per reinforcement) either after each reinforcement or following a specific number of reinforcements until the animal fails to respond for some criterion period of time. The last ratio successfully completed is then defined as the breaking point. In two early reports [8,9] rats were initially baselined on a progressive ratio 2 and 5 (PR2 and PR5) schedule, respectively, until the animals "showed no significant change in breaking point for several sessions." These authors reported reliable increases in breaking point with either increases in the concentration or volume of sweetened condensed milk delivered as the reward for a bar press response. Other investigators, [11] reported similar effects using electrical intracranial stimulation as the reward. Two studies [4,14] utilized a progressive ratio schedule of reinforcement to assess the relative reinforcing efficacy of intravenously self-administered drugs. These investigators found that cocaine maintained higher breaking points than several other drugs including methylphenidate and secobarbital; however, attempts to differentiate between unit doses (i.e., dosage per injection) of the same drug met with mixed success. In a more recent study [5], higher unit doses of cocaine tended to maintain higher breaking points, up to about 0.4 mg/kg/infusion. Unit doses above 0.4 mg/kg tended to engender breaking points below those obtained with 0.4 mg/kg/infusion, but higher breaking points than those produced the unit doses below 0.4 mg/kg.

The progressive ratio procedure reported here differs considerably from that of others [4, 5, 14]. These investigators baselined (schedule of reinforcement the animals were maintained on between successive progressive ratio tests) their animals on a moderately large fixed ratio (FR) schedule of reinforcement, i.e., a constant number of responses were required for reinforcement whereas the animals in the present experiment were baselined on a continuous reinforcement schedule (CRF), i.e., each response is followed by a reinforcement, between tests. Furthermore, their studies [4, 5, 14] utilized large increments (approximate doubling of the response requirement after each reinforce-

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ment) while the present experiment utilized a gradually accelerating increase in the response requirement. Finally, the present experiment used a sliding criterion for determining breaking points as opposed to the fixed criterion used by others [4, 5, 14]. This criterion was based upon the average interesponse time engendered by each unit dose during the baseline period which preceeded progressive ratio tests.

The 3 experiments reported here were undertaken to answer several questions. First, could the size of the increments utilized by others [4, 5, 14] explain why their procedures failed to adequately discriminate between different unit doses of the same drug? Experiment 1 addresses this question by utilizing a more gradual increase in the ratio requirement than previously reported [4, 5, 14]. Second, since the results of Experiment 1, reported below, were not as consistent as those reported by other investigators utilizing more traditional rewards, Experiment 2 was conducted to determine whether this lack of consistency was a result of procedural variations. More specifically, would a traditional appetitive reward studied under the same baseline schedule and progressive ratio procedure used in Experiment 1, produce results similar to those reported by others [8]? Finally, since a primary motivation for devising a procedure to measure the reinforcing efficacy of drugs is to allow investigators to screen compounds for their potential abuse properties, the amount of time required to make a comparison between two drugs or two different unit doses of the same drug is of economic interest. Therefore, Experiment 3 was conducted utilizing a shorter baseline experience in order to determine the importance of the extended baseline experience used in Experiment 1.

EXPERIMENT 1

METHOD

Animals

The animals were experimentally naive male rhesus monkeys *(Macacca mulatta)* weighing approximately 4–5 kg at the start of the experiment. The animals had free access to water and were fed monkey chow (Wayne) twice daily. The monkeys were surgically prepared with chronic silicone rubber catheters (Silitube, Rodhelm-Reiss Inc., Belle Mead, NJ, 02502), which passed through either the internal jugular, external jugular or the femoral vein to the level of the right atrium. More detailed descriptions of the surgical procedure have been reported elsewhere [3,13].

Apparatus

Each animal was fitted with a metal harness [13], which was connected to a hollow spring (E & H Engineering, Chicago, IL), which was in turn connected to the back wall (25 cm above the floor) of the experimental enclosure which measured 91×91×121 cm. The animals were individually housed in these enclosures 24 hr per day until completion of the experiment. Two primate response levers (BSR, Beltsville, MD, 20705) were mounted on one wall 43 cm above the grid floor. Three panel lights (red, green, blue) were located 10 cm above each lever. Ambient illumination was provided during the experimental session by a 7 W incandescent houselight. A ventilation fan provided continuous air exchange and masking noise at approximately 70 dba. One-half sec, 0.5 ml infusions of either saline or saline drug solutions were administered by means of a peristaltic type infusion pump (Masterflex®, Cole-Palmer, Chicago, IL) through vinyl tubing which passed through the hollow restraint arm. Within the back of the harness the tubing was connected to the catheter which exited the animal's back under the harness. Experimental contingencies were programmed automatically by electromechanical programming equipment located in a separate room. Data were recorded on cumulative records and from impulse counters.

Procedure

Four-hour experimental sessions were conducted daily, 7 days per week. The onset of each session was indicated by the illumination of the blue light over the right hand lever and the houselight. Responses on the right lever had no programmed consequences. Each animal was initially conditioned to press the left hand lever by making a 0.2 mg/kg infusion of cocaine hydrochloride contingent on each lever press. Following acquisition of the lever press response the animals were baselined under 4 hr daily limited access conditions on a continuous reinforcement schedule (CRF) for 1 of 6 unit doses of cocaine hydrochloride (0.025, 0.05, 0.1, 0.2, 0.4 and 0.8 mg/kg) for 5–7 days, at which time self-administration behavior had stabilized as determined by visual inspection of the cumulative records. The order of dosage testing was randomized for each animal and each animal was tested with 5 of the 6 doses.

Following stabilization of self-administration behavior with a unit dose the animal was tested under a progressive ratio procedure with the following conditions: (1) For the first 32 reinforcements obtained, the response requirement was increased by 1 following each reinforcement. (2) For the next 16 reinforcements, the response requirement was increased by 2 following each reinforcement. (3) For the next 16 reinforcements, the response requirement was increased by 4. (4) Following each additional set of 16 reinforcements, the number of responses added to the schedule requirement per reinforcement was doubled. Table 1 presents the schedule of increases followed until an animal failed to respond for a period of time equal to 3 times his longest interresponse time (IRT) for the three baseline sessions immediately preceeding the progressive ratio test. This ratio was defined as the breaking point in the present study. If an animal failed to reach a breaking point on the first day of testing, the program was continued on the following day where the animal left off. On the day following a breaking point determination, baselining for a different unit dosage was initiated.

RESULTS

Average response rates for the three days preceeding progressive ratio testing at all doses utilized in all animals are shown in Fig. 1. With the exception of one animal (070) similar unit doses engendered very similar rates of responding, suggesting that none of the animals displayed significant differences in sensitivity to the reinforcing or rate disrupting actions of cocaine. Response rate and unit dosage were inversely related.

Breaking points for all animals at all unit doses are presented in Fig. 2. Examination reveals two important points: Generally speaking, larger unit doses tended to produce higher breaking points within a particular animal. The wide variation observed in absolute breaking points would not have seemed likely given the similarity in baseline response

TABLE 1

Increment Size	Order of Fixed Ratios Presented					Cumulative Reinforcement Number
1	1,	2,	3,	4, . . .	32	1- 32
2	34,	36,	38,	40, . . .	64	33- 48
4	68,	72,	76,	80, . . .	128	49- 64
8	136,	144,	152,	160, . . .	256	65- 80
16	272,	288,	304,	320, . . .	512	81- 96
32	544,	576,	608,	640, . . .	1024	97-112
64	1088,	1152,	1216,	1280, . . .	2048	113-128
128	2176,	2304,	2432,	2560, . . .	4096	129-144
256	4352,	4608,	4864,	5120, . . .	8192	145-160

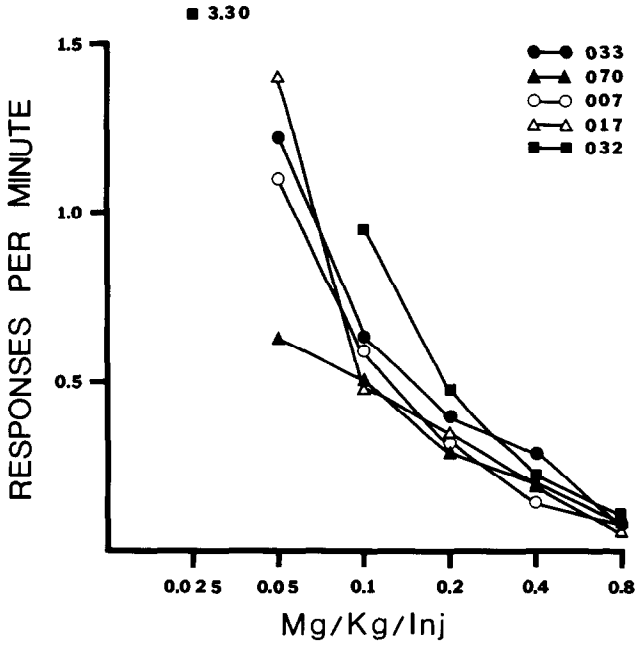

FIG. 1. Response rates for each animal as a function of dose per injection. Animal 032 was the only animal tested at the 0.025 mg/kg unit dose. The 3.3 point for Animal 032 at the 0.025 mg/kg unit dose refers to responses per minute.

rates across animals within a given dose. There is considerable variability in the absolute breaking point for a given unit dose across animals (i.e., 0.4 mg/kg, FR 15-3712). In 3 of the 5 animals tested, the 0.8 mg/kg unit dose engendered a breaking point lower than the 0.4 mg/kg dose. This would tend to suggest that the reinforcing efficacy function across unit doses that are self-administered has an inverted U-shape rather than sigmoidal as might have been expected.

DISCUSSION

The response rate unit dose functions are quite comparable to that collected by one of the present authors at another laboratory [12], and by other investigators at other laboratories. This fact lends credence to the notion that procedural variations rather than situation variables were responsible for the differences between the progressive ratio data reported here and that of others.

The breaking point criterion selection for the present study differed significantly from that utilized by others. In an earlier report [8], a period of 15 min of no responding was used while others [4,5] report using a criterion of a 24 hr period of no responding. The criterion for the present studies (three times an animal's longest IRT for the baseline sessions immediately preceeding the progressive ratio test) was selected to take into account the immediate effects of cocaine on cocaine-reinforced responding. It is well established that the response rates engendered by intravenous cocaine on a CRF schedule under limited access conditions are inversely related to the size of the unit dose. Furthermore, responding is quite uniform throughout a session. Procedures using a fixed duration criterion, which is short relative to the IRT's engendered by a given dose, would tend to artificially decrease the breaking points for higher unit doses; whereas a long duration criterion would tend to artificially inflate the breaking points for smaller doses. Therefore, the sliding criterion reported here was selected to take into account the rate decreasing effects of cocaine on cocaine-reinforced responding.

The breaking points obtained herein generally support data presented by others [4, 5, 14]. One of these investigators [14] reported that larger unit doses of cocaine (0.03, 0.12 and 0.48 mg/kg) maintained higher progressive-ratio performance than lower unit doses within this dosage range. The present data over this same dose range demonstrated the same functional relationship between breaking point and unit dosage even though the procedures differed significantly. The other investigators [15] also reported increases in breaking point with increases in the unit dose at or below 0.4 mg/kg. However, above 0.4 mg/kg/inj. these authors report no consistant relationship between breaking point at the 0.4 and 0.8 mg/kg unit doses. This lack of consistency of breaking points seen with higher unit doses of cocaine supports the results of another self-administration study [10], in which a choice procedure also failed to demonstrate preferential responding when animals had to choose between these higher unit doses. These authors did report that over a lower range of unit doses, animals would choose the larger of two unit dosages.

Although, in the present study, higher unit doses tended to maintain higher breaking points, the data are not all com-

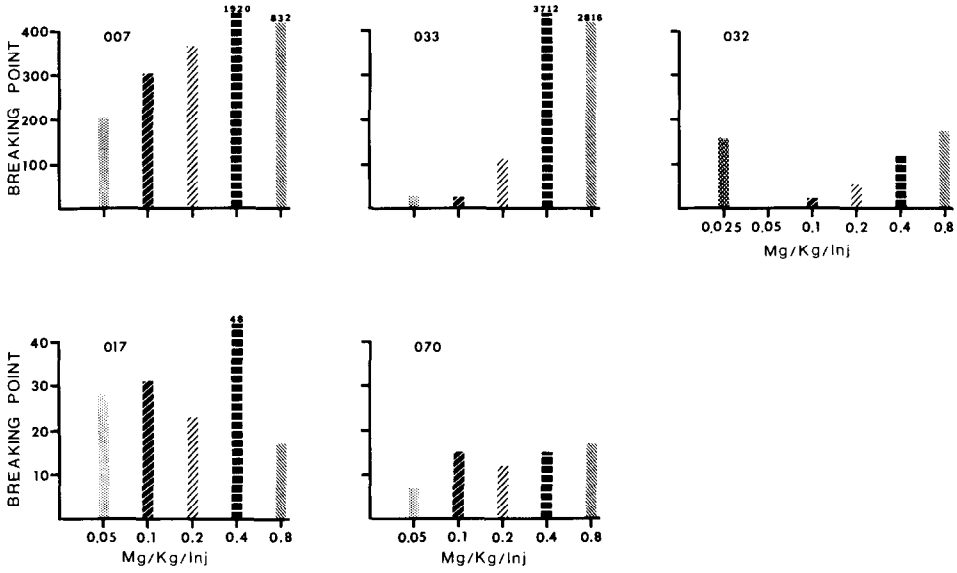

FIG. 2. Breaking points for each animal as a function of dose per injection. Arabic numbers at the top of some of the bars represent the breaking point for that dose. The reader should note that two different ordinate scales are used.

parable, with respect to consistency, to the data reported by others for progressive ratio behavior maintained by more traditional reinforcers [9]. Several possible explanations might account for this discrepancy: (1) Intravenous cocaine may simply be a marginally reinforcing stimulus although at least in some of the animals reported here, the high ratios achieved tends to mitigate against this explanation. (2) Unit dose differences may be diluted at lower ratio values since the animal could quickly self-administer several small doses possibly producing a blood level and effect comparable to that produced by a single injection of a higher unit dose. (3) The procedure reported here differs significantly from an earlier report [7], which might also account for the lack of consistency. Therefore, Experiment 2 reported below was conducted utilizing a more traditional appetitive reward to determine if procedural dissimilarities could account for the observed differences.

EXPERIMENT 2

METHOD

Animals

Two of the monkeys (007, 033) that served in Experiment 1 were used in the present experiment. The third monkey (045) had served in an unrelated behavioral study. Animals were drug free for at least 2 months preceeding this study. All other factors including food and water availability relating to animal description were the same as in Experiment 1 except that the animals were no longer catheterized.

Apparatus

Animals were fitted with the restraining arm and harness described previously and were individually housed in sound attenuating experimental chambers similar to those described in Experiment 1. However, a liquid delivery cup replaced the right hand lever [1]. Tang® (General Foods) was delivered through vinyl tubing which connected the peristaltic pump (previously described) to the delivery cup.

Procedure

Two different series of reinforcers were tested in this experiment. The first series consisted of 0.5, 2.0, 4.0 and 8.0 ml vol. of a 70 mg/ml solution of orange-flavored Tang® maintained at room temperature. This concentration closely approximates the manufacturer's recommended concentration for human consumption. The order of testing of the different volumes was randomized for each animal and all volumes were tested in each animal. The second series consisted of a 35, 70 and 140 mg/ml solutions of Tang® with the volume held constant at 2.0 ml. As in the first series the solutions were maintained at room temperature and the order of testing of the three concentrations was randomized for each animal.

Four hour experimental sessions were conducted daily 7 days per week. The animals were baselined on a CRF schedule for a minimum of 7 days or until responding was stable as determined by visual inspection of their cumulative records. Following achievement of stability the progressive ratio procedure described in Experiment 1 was in effect until a breaking point was attained. Breaking point in this study was defined as not responding for 15 min [8]. Progressive ratio sessions lasted 7 hr instead of the 4 hr utilized during baseline, in an attempt to obtain breaking points in 1 session. The series of volumes was tested first followed by the concentration series.

RESULTS

Average response rates for all animals at all reinforcement volumes are presented in Fig. 3. Although there was considerable intersubject variability with respect to response

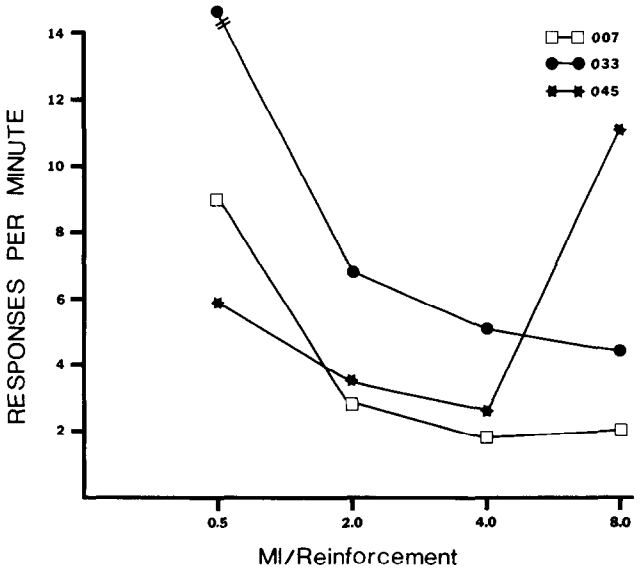

FIG. 3. Response rates for each animal as a function of reinforcement volumes of Tang® tested.

rate at any given volume, in general as the reinforcement volume was increased the response rate decreased.

The data from the progressive ratio tests for the different volumes are presented in Fig. 4. Data from two of the 3 animals (045, 033) clearly support the hypothesis that the greater the reinforcer magnitude, the greater the reinforcing efficacy as defined by higher breaking points. The third animal (007) evidenced similar breaking points across all volumes. Animals 045 and 033 demonstrated breaking points for the 8.0 ml volume substantially below the 4.0 ml volume.

Response rates tested at the different concentrations did not demonstrate any appreciable differences across concentrations. Likewise, there was no systematic relationship demonstrated between concentration and breaking point. Only one of the animals demonstrated an increase in the breaking point with increases in the Tang® concentration.

DISCUSSION

The response rate—reinforcement volume functions are in agreement with the unit dose versus response rate function previously demonstrated with intravenous cocaine. This decreasing rate seen with increasing volume is probably a result of one or two factors: (1) As the volume of the reinforcer was increased, the amount of time required to ingest the Tang® was increased, thereby producing a decrease in overall response rate. (2) Onset of satiation may have been more rapid as the volume was increased which would also produce a decrease in overall rate. However, the data for animal (045) at the 8.0 ml volume seems to contradict this explanation, since the highest rate was engendered by the largest volume. Response decrements with large amounts of reinforcement such as those seen with animals 033 and 007 have been reported by others [2,7] and the most likely explanation seems to be that there is an interaction between performance and satiation, with satiation producing smaller effects at the smaller volumes. Analysis of the baseline records for the session preceeding each progressive ratio test showed significantly more responding in the first half of the session than in the last half indicating some satiation was occurring. However, no consistent relationship between time of onset of satiation effects and the reinforcer volume was observed.

The decrease in the breaking point observed at the 8.0 ml volume would appear to be best explained by the performance-satiation interaction alluded to above. Other investigators [9] studying several volumes of sweetened milk under a progressive ratio procedure with rats also noted a decrease in the breaking point at the highest volume. These authors also interpreted the effects to be a result of satiation and specifically tested this assumption utilizing a progressive ratio which minimized satiation effects. By using a PR 40 regime (i.e., response requirement was increased by 40 after each reinforcement) these authors were able to keep the overall amount of liquid consumed per session low, thereby eliminating potential effects of satiation. The results of this experiment [9] clearly support the satiation explanation for the lower breaking points at the large volumes, since the largest volume in this study engendered the highest breaking point.

The lack of any consistent relationship between Tang® concentration and response rate or breaking points is puzzling since other investigators [8] have reported increases in the breaking point obtained with increases in the concentration of sweetened condensed milk. One possible explanation for the inconsistencies observed here is that the range of concentrations in the present study was either too high or too low. No preliminary preference testing was undertaken and the human concentration suggested by the manufacturer may be quite inappropriate for the non-human primate.

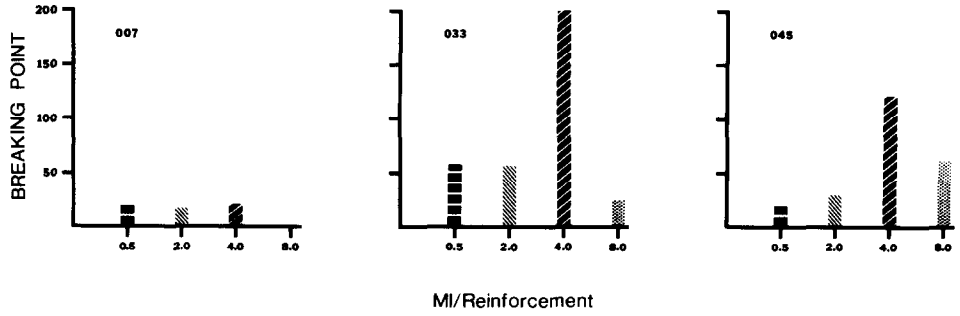

FIG. 4. Breaking points for each animal as a function of each volume of Tang® tested.

EXPERIMENT 3

METHOD

Animals

The animals for this experiment were five male rhesus monkeys *(Macaca mulatta)* weighing between 3.5 and 5.0 kg. Four of the animals were experimentally naive and the fifth had received one dose of diazepam [6]. All animals were drug free for at least 3 months prior to this study and none had had prior exposure to cocaine or to the progressive ratio procedure. Otherwise, animals were housed and treated identically as in Experiment 1. The same apparatus used in Experiment 1 was used in this study.

Procedure

The procedure used here was similar to that reported for Experiment 1 but with several exceptions. First, session duration was increased from 4 to 6 hr. Second, breaking point was defined as not having responded for 1 hr. Third, the animals baseline experience, preceding the PR test, consisted of 50 reinforced responses at the appropriate unit dose. The animals were all initially trained with the 0.2 mg/kg dose and allowed to self-administer 50 reinforcements. After the animal had received 50 such reinforcements, the unit dosage was randomly switched to one of four other unit doses (0.05, 0.1, 0.4, 0.8 mg/kg). The animal was then allowed to self-administer 50 reinforcements at the new dose. On the day following the session in which the animal obtained the 50th reinforcement, the animal was switched to the standard progressive ratio procedure described in Experiment 1. The initial unit dose tested following acquisition of bar pressing behavior was randomly determined for each animal as were the remaining sequence of 4 unit doses. Each unit dose was tested at least twice (except where noted) in each animal in separately randomized sequences.

RESULTS

The data from this group of progressive ratio animals is presented in Fig. 5. From this figure it would appear that this procedure discriminates reinforcing efficacy about as effectively as the procedure used in Experiment 1 reported above. Four of the five animals generally displayed an increase in breaking point with increases in the unit dose. However, the bars on these graphs represent the median breaking point for each animal at each dose. The median was selected as the measure of central tendency to represent these data because of the extreme variability displayed by some of the animals. Table 2 presents the mean, median and standard errors for the breaking points produced by these animals. As can be seen from the table, with the exception of animal (111), all of the animals displayed considerable variability at one or more of the doses tested. Animal 116, in which only one determination was obtained at each dose, died before completion of his first series. A necropsy, performed immediately after death, did not reveal any specific pathology that might account for his death.

DISCUSSION

It will be recalled that the three prominent changes employed in this experiment compared to Experiment 1 were: (1) baseline session length was increased from 4 hr to 6 hr; (2) baseline experience consisted of 50 reinforced responses; (3) breaking point was defined as not having responded for 1 hr for all doses tested. Session duration was increased so that at all doses except 0.8 mg/kg, the animals would self-administer the criterion 50 reinforcements in one session. It is unlikely that this procedural change would have produced the effects observed during the progressive ratio tests. The change in the breaking point criterion, on the other hand, might be expected to have a substantial effect. Previous investigators utilizing progressive ratio procedures [4, 5, 8, 9] have all

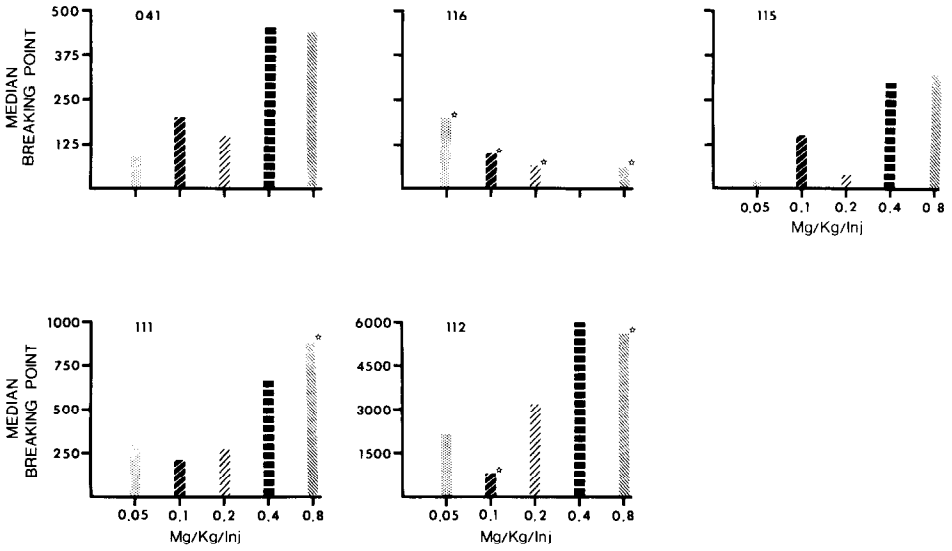

FIG. 5. Median breaking points obtained from each animal as a function of dose per injection tested. *—Indicates only one determination was made at that unit dose. Animal 116 died before completion of the first series. The reader should note that three different ordinate scales are used.

TABLE 2

MEAN, MEDIAN, AND STANDARD ERROR FOR THE BREAKING POINT DETERMINED FOR EACH ANIMAL AT EACH UNIT DOSE TESTED

Animal		Dose mg/kg/injection 0.05	0.1	0.2	0.4	0.8
111	Mean	302	258	398	576	896
	Median	302	240	268	672	*
	St. Error	178	49.4	125.3	112.4	*
112	Mean	2176	832	3200	6016	5632
	Median	2176	*	3200	6016	*
	St. Error	896	*	0	1920	*
115	Mean	72	808	731	378	309
	Median	72	144	32	288	320
	St. Error	40	684	694	98.8	157.4
041	Mean	80	200	152	456	442
	Median	80	200	160	456	442
	St. Error	48	72	48.7	24	358
116	Mean	208	108	64		64
	Median	*	*	*		*
	St. Error	*	*	*		*

*—Indicates only one determination was made at that unit dose.

utilized a fixed criterion. As was discussed earlier fixed criteria (dependent on whether they are long or short relative to average interresponse times-IRTs) tend to bias one end of the dosage range or the other, whereas a sliding scale based upon average IRTs controls for this bias. The 1 hr fixed criteria was selected because it was as long or longer than any of the criteria utilized in Experiment 1. Selecting a criterion in this way allowed for a retrospective analysis of the data from this experiment utilizing, effectively, the criteria used in Experiment 1. A comparison between breaking points obtained using the fixed 1 hr criterion and those obtained using the sliding criterion demonstrated no major shifts in the shape of the dose vs. breaking point functions. The final procedural change adopted in this experiment, the elimination of the extended (7–10 days) baseline experience prior to each progressive ratio test, apparently was responsible for the extreme intrasubject variability, engendered by this procedure, in the dosage-breaking point relationship. It is unclear at this point why extended CRF experience prior to the progressive ratio test would be important since the discriminability of individual unit doses is easily demonstrable. A recent study [10] utilizing a choice procedure clearly showed that rhesus monkeys will preferentially select the higher of two unit doses indicating an ability to differentiate between them.

In summary, the progressive ratio procedure reported here appears to have some validity in assessing the relative reinforcing efficacy of intravenously self-administered drugs. Although absolute breaking points reported here differed substantially from those reported by others [4, 5, 14], the relationship of breaking points within the dosage range tested in this study and similar ranges tested by other investigators is in agreement even though there were considerable procedural differences between the present experiments and those reported by others. In addition, the decrease in breaking point above 0.4 mg/kg is in agreement with results from the choice procedure discussed earlier [10].

The intersubject variability observed with the present procedure appears to be somewhat greater than that observed by others [8,9] using more traditional appetitive rewards. However, assessment of the overall intersubject variability obtained by these other investigators was not possible. The data reported in Experiment 2 demonstrated that the procedure can discriminate differences in reinforcer magnitude when traditional rewards are used and is sensitive to the same variables (i.e., satiation effects) as those procedures reported by other investigators using similar rewards.

Experiment 3 was an attempt to shorten the amount of experimental time required to test a series of dosages for their relative reinforcing efficacy. These attempts were met with mixed success with the principle problem being excessive within-animal variability. As only one breaking point determination was made at each dose in Experiment 1, it was not possible to make a comparison between the two procedures on this point. However, from the analysis of the data available it was concluded that the short baseline experience given at each unit dose was the most likely reason for the inconsistencies observed. It would appear, however, that there should be some intermediate amount of baseline experience that would produce consistent breaking point-reward magnitude functions and still minimize the time required to test several doses of a drug. Future research concerning the use of this progressive ratio procedure to measure relative reinforcing efficacy should be directed toward determining those factors responsible for the variability observed with the present procedure. The recent study [5] in which baboons were tested with a progressive ratio procedure for intravenous drug reinforcement reported much less variability, a fact which appears to support the use of procedures which minimize the ability of animal to sum dosages. However, we feel that the data generated by the present procedures support the use of smaller increments in the response requirement.

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REFERENCES

1. Bedford, J. and M. Wilson. A technique for converting from intravenous drug self-administration to liquid reinforcement. *Behav. Res. Meth. Instrum.* **10:** 99–100, 1977.
2. Conrad, D. and M. Sidman. Sucrose concentration as reinforcement for lever pressing by monkeys. *Psychol. Rep.* **2:** 381–384, 1965.
3. Deneau, G. A., T. Yanagita and M. H. Seevers. Self-administration of psychoactive substances by the monkey. *Psychopharmacologia* **61:** 30–48, 1969.
4. Griffiths, R. R., J. A. Findley, J. V. Brady, K. Guther and W. Robinson. Comparison of progressive ratio performance maintained by cocaine, methylphenidate and secobarbital. *Psychopharmacologia* **43:** 81–83, 1975.
5. Griffiths, R. R., J. V. Brady and J. D. Snell. Progressive-ratio performance maintained by drug infusions: comparison of cocaine, diethylpropion, chlorphentermine, and fenfluramine. *Psychopharmacology* **56:** 5–13, 1978.

6. Grove, L., M. Wilson and J. Bedford. Effects of diazepam on food competition in the rhesus monkey. *Pharmacologist* **18:** 228, 1977.
7. Guttman, N. Equal reinforcement values for sucrose and glucose solutions compared with equal sweetness values. *J. comp. physiol. Psychol.* **47:** 358–361, 1954.
8. Hodos, W. Progressive ratio as a measure of reward strength. *Science* **134:** 943–944, 1961.
9. Hodos, W. and J. Kalman. Effects of increment size and reinforcer volume on progressive ratio performance. *J. exp. Analysis Behav.* **6:** 387–392, 1963.
10. Johanson, C. and C. R. Schuster. Choice procedure for comparing drug reinforcers: Cocaine and methylphenidate in the rhesus monkey. *J. Pharmac. exp. Ther.* **193:** 676–688, 1975.
11. Keesey, R. E. and M. D. Goldstein. Use of progressive fixed ratio procedures in the assessment of intracranial reinforcement. *J. exp. Analysis Behav.* **11:** 293–301, 1968.
12. Wilson, M. C., M. Hitomi and C. R. Schuster. Psychomotor stimulant self-administration as a function of dosage per injection in the rhesus monkey. *Psychopharmacologia* **22:** 271–281, 1971.
13. Yanagita, T., G. Deneau and M. H. Seevers. Evaluation of pharmacological agents in the monkey by long-term intravenous self or programmed administration. *Experta Medica Int. Congr. Ser. No.* **87:** 453–457, 1965.
14. Yanagita, T. An experimental framework for evaluation of dependence liability of various types of drugs in monkeys. *Bull. Narcot.* **1:** 25–57, 1973.