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Cocaine Self-Administration in Monkeys by Chewing and Smoking [1,2]

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Cocaine Self-administration Coca-chewing Coca-smoking Smoking behavior

A number of investigators have studied cocaine self-administration in infrahuman primates by employing intravenous (IV) techniques since the rapid absorption by this route may be relevant to the intranasal route as well as the less common IV route used by man [cf. 34]. While such studies are important in understanding the reinforcing properties of cocaine, they fail to provide an appropriate animal model for studying the more widespread patterns of coca leaf chewing in the Andean regions of South America [11,14]. Indeed, the recent application of orally administered cocaine for treatment of human depression [21,22] underlines the need for animal studies which parallel these routes of administration. The development of an infrahuman primate model of self-administration by chewing would be highly useful in the study of these and related drug taking behaviors such as the chewing of tobacco, Betel nut and qat. In addition, the study of cocaine self-administration in infrahuman primate smoking models [cf. 15] might provide an alternative to intravenous administrations which still retains rapid absorption characteristics. Such a model as the latter would still be based on anthropological and historical uses of coca smoking [4,9] as well as on our observations of growing patterns of illicit cocaine smoking in North, Central and South America.

The topography of both the coca chewing response and the cocaine smoking response are relatively unknown phenomena compared to the more widely investigated intravenous procedures. Therefore, we have chosen to include a discussion of preliminary studies of these responses as well as the rationale for and development of vehicle and dose parameters used in the general procedures which follow. These pilot studies are important in understanding the relevance of the animal models of self-administration presented here to those related methods employed by man.

CHEWING STUDIES

Pilot Studies and Development of Methods

Topography of Response. According to Hanna [14] coca chewing resembles tobacco chewing in that a wad of leaves is placed in the mouth and chewed until compacted into a ball or quid, which is subsequently held in one cheek and periodically rechewed. Approximately 80% of the cocaine in the leaves is extracted by chewing while the juice and up to 70% of the leaves may eventually be swallowed. There is considerable evidence that coca leaf chewing produces cocaine-like physiological and psychological effects and that chewing small quantities over a long period of time avoids both undesirable side effects and habituation [14].

Choice of Vehicle. In a series of pilot studies with 4 male rhesus monkeys (approximately 2 years old, 10 kg), the topography of the chewing response was studied with both periphery wax [cf. 26] and plain gum base vehicles. The wax was not consistently chewed by all animals when given repeated presentations, and chewing time per unit weight

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showed large variance between the within animals. The plain gum base was chewed by all animals and the average chewing time over 60 discrete presentations was 400 sec per g of base, increasing linearly with weight of gum base. The animals frequently held the gum in their cheeks and periodically rechewed the pieces. Almost all pieces were swallowed after a minimum of 120 sec and base material was found in subsequent feces collections. The addition of cocaine hydrochloride to the gum vehicle resulted in a linear decrease in mean chewing time as a function of dose. In order to disguise the bitterness of the cocaine, a 0.8 gram piece of assorted flavor coated flavored gum ("Chiclets": Warner-Lambert Company) was chosen as the vehicle for these studies. Plugs of cocaine hydrochloride (5.0 mg) were inserted into the pieces with a dental amalgam carrier. This resulted in a preparation which was chewed by all animals for 250–400 sec and subsequently swallowed.

Calculation of Dose. Hanna [14] reports that in Peru the mean daily coca leaf consumption by chewing is 58 g per adult and this amount contains approximately 250 mg of available cocaine, or 5.2 mg/kg per day for people in his sample. Other studies reviewed by Hanna estimate daily consumption to be as high as 210 g per adult, or 18.86 mg/kg using Hanna's calculations. The pattern of chewing lasts for 2–3 hr at a time [34] but may continue virtually constantly throughout the day [11]. Gutierrez-Noriega and Von Hagen [13] report that the amount of cocaine alkaloid ingested per min of chewing is approximately 0.9 mg, while Chamochumbi [5] reports 1–1.5 mg per min from an initial 20 g of coca leaves. Based on these data, we attempted to provide our monkeys (approximate weight of 5 kg) with a total daily cocaine intake of 20 mg/kg which could be reached by chewing for 100 min. This dose is comparable to the highest regular human dose reported.

Since the ratio of coca leaf weight to available cocaine/kg is approximately 10,000:1, the total weight of gum based used here should have been approximately 200 g per day. However, in order to maximize potential reinforcing properties and to overcome the monkeys' natural aversion to chewing large quantities of gum base per day, we reduced this ratio to 10:1. Thus, monkeys in the initial study could earn 20 pieces of gum per daily session, each piece containing approximately 0.8 g gum and 5.0 mg cocaine hydrochloride (Mallinckrodt). Companion studies with an enzyme multiplied immunoassay technique for benzoyl ecgonine indicated significant urine levels of this cocaine metabolite after chewing of such pieces. Indeed, urinary benzoyl ecgonine levels increased linearly with the total cocaine gum chewed as presented in Table 1. By weight, the percentage of cocaine present in the gum was equivalent to that found in coca leaves [cf. 3,35].

For studies involving an active placebo, procaine was selected because of its similarlity to cocaine hydrochloride. Among the many synthetic local anesthetics found in illicit samples of cocaine, procaine is commonly used [20] and the most similar to cocaine in properties such as bitterness and benumbing sensations without accompanying side effects like sleepiness often associated with lidocaine use [28]. While procaine does not share cocaine's powerful effect on the cortex, like all local anesthetics it does stimulate the central nervous system. In order to minimize these CNS effects, the relatively insoluble procaine base was used here instead of the more soluble and rapidly absorbed procaine hydrochloride. Human observers judged 10 mg procaine base to be equivalent to 5 mg cocaine hydrochloride in bitterness and benumbing sensations, but without the latter's psychoactive effects.

TABLE 1

URINARY BENZOYL ECGONINE LEVELS (μg/ml) AND TOTAL AMOUNT OF COCAINE HYDROCHLORIDE CHEWED BY EACH MONKEY. EACH PIECE OF COCAINE GUM CONTAINED 5 mg OF COCAINE HYDROCHLORIDE

Cocaine gum (mg)	Urinary benzoyl ecgonine (μg/ml) Pearl	Lightning
25	0.60	0.65
50	0.72	0.80
75	1.11	1.31
100	1.70	2.15

General Procedures

Two female rhesus monkeys were individually trained in an operant unit (1m × 1m × 1m) equipped with 2 levers (right and left side of front panel), cue lights located over each lever, and a gum delivery chute below each lever. The chutes were connected to separate universal feeders (Ralph Gerbrands Company, Model 120) and all programming was controlled by conventional electromechanical and solid-state equipment. A voice-activated relay circuit recorded animal vocalizations in the range of 0.5–1.5 kc and at least 0.2 sec in duration. An amplifier circuit operating through a phonograph cartridge transducer recorded animal locomotor activity in the operant unit.

The animals were trained according to the following general procedure. During a 5 min intertrial interval (ITI), a single white light located over the center of a lever was illuminated and responses had no programmed consequences. A trial began when the white light and a side colored light were illuminated. A red side light was paired with gum vehicle only (plain gum), a green light with vehicle plus cocaine (cocaine gum), and a blue light with vehicle plus procaine (procaine gum). Completion of a fixed ratio 10 (FR10) delivered 1 piece of gum to the chute signaled by a brief white light located over the chute. Additional lever responses at this point had no programmed consequences. When a photo-cell circuit indicated that the monkey had removed the gum from the chute, the ITI began. When a single lever was available in a session, lights over the other lever were dark. The availability of the right or left lever was randomly alternated between sessions. When both levers were available within a session (choice tests discussed below), lights over both were illuminated and extinguished at the same times. In such 2 lever sessions, responses on one lever did not accumulate on the other and independent FR 10 schedules were required. Once a reward was delivered, responses on the other lever had no programmed consequences. Responding on both levers remained ineffective until the end of the ITI when cue lights were again illuminated and new FR 10 schedules were required with no savings of previous responses.

Initially, the monkeys were deprived of their normal diet of Purina monkey chow pellets for 21 hr and trained to respond for pellets. Gum was gradually substituted for the pellets until only gum was available during the session. At the end of each session, animals were supplemented in their home cages with pellets and fresh fruit. Water was freely available in the home cage and, in later studies, in the operant unit as well.

Self-Administration Behavior

After several sessions with plain gum vehicle, both monkeys were earning most of the 20 pieces available within a maximum 2 hr session, and performance stabilized with less than a 10% daily change in responses. Sample cumulative records are shown in Fig. 1. Here it can be seen that both monkeys, Pearl and Lightning, executed the FR 10 immediately following the ITI with little or no responding during the ITI. Monkeys removed the gum from the chute upon delivery and no discarded gum was observed on the floor or in the unit at the end of the sessions. During one block of 7 consecutive sessions with plain gum, Pearl and Lightning had mean ITI rates of .23 responses per min (rpm) and .52 rpm, respectively. Pearl emitted a mean .29 vocalizations per min (vpm) and Lightning emitted .74 vpm during these same sessions. The majority of these sounds occurred in the ITI and appeared to be food barks or food calls which are given in response to the sight and sound of food [25].

During a subsequent block of 7 consecutive sessions with procaine gum, there were no substantial changes in responding as indicated by the sample records in Fig. 1. Mean ITI rates here were .23 rpm for Pearl and .28 rpm for Lightning. Mean voclizations were .43 vpm for Pearl and .88 vpm for Lightning.

The records in Fig. 1 illustrate the several dramatic changes which occurred in a subsequent block of 20 sessions during which cocaine gum was available. Pearl showed a disruption in stimulus control as her mean ITI responding increased to 1.43 rpm and FR responding, particularly near the end of the sessions, was interrupted with frequent pauses. Lightning's records showed less disruption with a mean .33 rpm during the ITI. However, Lightning did exhibit an increased latency to respond after the ITI. It was during these cocaine sessions that uneaten and partially chewed gum was first observed on the floor of the operant unit. Both monkeys discarded approximately 5% of their delivered gum in this way. Interestingly, vocalizations decreased for both animals during cocaine sessions with means of .15 vpm for Pearl and .29 vpm for Lightning.

Choice Tests

A series of choice tests were conducted next in order to determine gum preferences. On any given session, 2 types of gum were available, one type on each lever. Appropriate colored lights signaled the identity of the gum available and the lever on which any given gum was available was randomly alternated between sessions. Four consecutive sessions were run on each of 3 choice situations: plain-cocaine, plain-procaine, and cocaine-procaine. Sessions were run until a total of 20 reinforcements were delivered or 3 hr elapsed, whichever event occurred first.

The results of these tests are presented in Table 2 in terms of the total number of gum pieces earned and discarded by each monkey in each choice test. The maximum number of pieces available over the 4 separate choice tests was 80. It is clear from this data that both monkeys preferred plain gum over either cocaine or procaine gum. In the test with cocaine-procaine, Pearl preferred procaine while Lightning preferred cocaine. Most of the discarded gum had been partially chewed but the impacted plug of cocaine or procaine was usually found intact. Taken together, these results are equivocal and do not suggest a preference for cocaine gum per se. Since the sweeter plain gum was preferred in most cases, it remains possible, therefore, that animals were responding on the basis of sweetness or bitterness rather than on the basis of psychoactive effects.

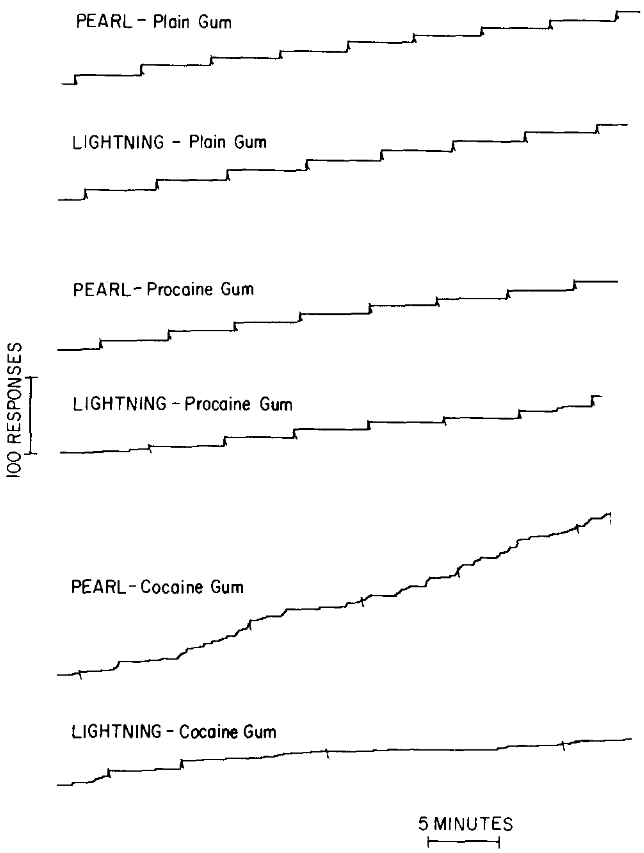

FIG. 1. Sample cumulative records of FR 10 responding for each monkey from sessions with either plain gum, procaine gum or cocaine gum.

Futher chewing studies are necessary in order to understand the differences in self-administration rates here compared to those seen for cocaine administered IV. As it stands now, the monkeys in the present studies did not prefer cocaine gum, although they did self-administer it in the block of 20 sessions prior to choice tests.

SMOKING STUDIES

Pilot Studies and Development of Methods

Topography of Response. One of us (RKS) has conducted a series of interviews with respondents who have smoked cocaine preparations in North and South America. In areas of Mexico and Peru, the preparation is called "base" [1, p. 331] and consists of hand-rolled cigarettes of tobacco *(Nicotiana tabacum* or *Nicotiana rustica)* and cocaine base (alkaloid). Layers of tobacco are alternated with layers of cocaine base and the cigarette is subsequently smoked with long inhalation techniques similar to those

TABLE 2

TOTAL NUMBER OF GUM PIECES EARNED AND DISCARDED (IN PARENTHESES) BY EACH MONKEY IN EACH CHOICE TEST OF FOUR SESSIONS

	CHOICE TEST					
	Plain Gum vs. Cocaine Gum		Plain Gum vs. Procaine Gum		Procaine Gum vs. Cocaine Gum	
Pearl	53 (4)	15 (3)	23 (1)	5 (2)	38 (8)	17 (8)
Lightning	73 (1)	5 (1)	23 (0)	17 (5)	7 (4)	34 (20)

TABLE 3

TOTAL PUFF DURATION (SEC) AND URINARY BENZOYL ECGONINE LEVELS (μg/ml) FOR EACH MONKEY SMOKING CIGARETTES CONTAINING 30 mg COCAINE BASE EACH

Alex		Phoebe		Pupi	
Puff Duration (sec)	Benzoyl Ecgonine (μg/ml)	Puff Duration (sec)	Benzoyl Ecgonine (μg/ml)	Puff Duration (sec)	Benzoyl Ecgonine (μg/ml)
10.0	0.00	10.0	0.00	10.0	0.00
50.0	1.50	50.0	0.65	50.0	0.60
100.0	2.00	100.0	2.44	100.0	1.37
778.0	3.25	1608.0	3.32	443.0	1.92

used with *Cannabis* preparations. Ashley [2] reports that cocaine is also sprinkled on the end of a tobacco cigarette or throughout a *Cannabis* cigarette. In California, our respondents remove the tobacco from commercial cigarettes and refill the paper tube with alternate layers of cocaine base and tobacco. The average "base" cigarette contains approximately 1.0 g cocaine base and is smoked by 2–3 persons over an average 4 hr period. Respondents report immediate psychoactive effects which compare favorably with the effects from IV administration.

Vehicle and Dose. In a series of pilot studies with three rhesus monkeys, cocaine base was mixed with *Lactuca sativa* (lettuce: Bravo Smokes, Inc., Hereford, Texas)in commercial cigarette paper tubes and smoking behavior was studied (see General Procedures below). It was determined that in a daily 1 hr session, the average smoking response (puff frequency and duration) of cigarettes containing 0.7 g lettuce and 30 mg cocaine base resulted in urine levels of benzoyl ecgonine approximately equal to those found after monkeys chewed 20 pieces (1 session) of cocaine gum (5 mg) used in the previous studies. Indeed, urinary benzoyl ecgonine levels were directly related to increasing puff durations on such cigarettes (Table 3). Thus, this preparation of lettuce and cocaine base was used in the present investigations. Three 10 mg plugs of cocaine base were inserted into each lettuce cigarette with a dental amalgam carrier. The plugs tended to be located near the middle of the cigarette.

General Procedures

Three adult rhesus monkeys (approximately 15 years old, 7.6 kg) were trained to puff on lettuce cigarettes according to a previously described procedure [15]. Briefly, the apparatus consisted of a large operant unit equipped with 2 stainless steel smoking tubes, one on each side of a centrally positioned solenoid-operated water delivery spout. A single white light was located above each tube and a green light was located above the water spout. The ends of the smoking tubes were flattened so that licking behavior and other components of the drinking response were physically prevented and the animal was required to suck or inhale smoke rather than lick smoke. Monkeys were trained to puff on one or the other smoking tube (indicated by white light) in order to gain access to a 1.5 ml water reward signaled by the green light. Puff duration was gradually shaped to 1000 msec and monkeys earned all their water in this manner in daily 1 hr sessions. Companion studies using In-113m labeled smoke indicated that some smoke was inhaled into the lungs via this procedure [24].

Initially, lettuce cigarettes were available on dispensers connected to each of the 2 tubes. The dispenser apparatus [23] positioned a cigarette behind a tube and ignited it. As the cigarette burned to within 10 mm of the end, a thermistor circuit rotated the dispenser, bringing a new cigarette into position and lighting it. A total of 30 cigarettes could be delivered to the animal in this way by each dispenser. Only 1 tube and its dispenser were available within a session, and tubes were randomly changed between sessions. Vacuum switches sensed puff duration while programming equipment recorded number of cigarettes, puffs, individual puff durations and rewards.

The experiment was conducted in 5 treatment blocks of 10 sessions each. The first block (Baseline) consisted of 10 successive daily sessions during which lettuce cigarettes were available on 1 dispenser only. Animals were water deprived and earned all of their daily water in these 1 hr sessions (with subsequent supplements in home cages if necessary). The second block (Baseline-Extinction) consisted of 10 successive daily sessions during which lettuce cigarettes were available on 1 dispenser and animals

TABLE 4

MEANS OF SMOKING MEASURES FOR EACH BLOCK OF TREATMENT SESSIONS FOR EACH MONKEY. CIGS = MEAN NUMBER OF CIGARETTES CONSUMED. WHEN MULTIPLIED BY 30, THIS FIGURE REPRESENTS AMOUNT IN mg OF COCAINE ALKALOID AVAILABLE IN COCAINE SESSIONS. PUFFS = MEAN NUMBER OF PUFFS PER SESSION. TIME = MEAN TOTAL DURATION OF PUFFING PER SESSION IN SEC.

Block	1 Lettuce	2 Lettuce-Water Ad Lib	3 Cocaine	4 Cocaine-Water Ad Lib	5 Choice Test Lettuce	Cocaine
Alex						
CIGS	4.7	4.0	5.0	6.6	7.2	7.4
PUFFS	142.4	27.2*	111.2†	97.8	27.6	73.8*
TIME	132.7	9.4*	66.7	46.5	19.3	24.8
Phoebe						
CIGS	5.6	0.6	10.5	6.4	4.7	7.7
PUFFS	240.4	0.06*	317.4	157.9*	47.9	132.3*
TIME	202.9	0.3*	192.5	89.3*	28.5	65.6*
Pupi						
CIGS	6.7	0.0	5.8	5.2	—†	—
PUFFS	353.1	0.0*	239.8	52.6*	—	—
TIME	373.9	0.0*	143.5	27.4*	—	—

*Significantly different from column to left at $p<0.05$ (paired t-tests).
†Represents sessions not run. Animal died from natural causes prior to this block.

received ad lib water in their home cages prior to each session. However, in these quasi-extinction sessions, the water reward delivery system was still operated so as to minimize disruption of stimulus control. The third block (Cocaine) consisted of 10 successive daily sessions during which cocaine cigarettes were available on 1 dispenser and animals were water deprived and earned water during these sessions. The fourth block (Cocaine-Extinction) consisted of 10 sessions prior to which animals were given free access to water in their home cages and during which cocaine cigarettes were available on 1 dispenser. The fifth block (Choice Test) consisted of 10 successive daily sessions during which both smoking tubes and their dispensers were available and animals were water deprived. One smoking tube permitted access to cocaine cigarettes while the other dispenser contained plain lettuce cigarettes. The position of cocaine and lettuce cigarettes was randomly changed between sessions. The 5 blocks of treatments were conducted over a period of 8 months with regular baseline sessions intervening between each block.

Self-Administration Behavior

The results from these smoking studies are presented in Table 4 in terms of the means of smoking measures for each block of treatment sessions for each monkey and the results of paired t-tests between blocks. Here it can be seen that all 3 monkeys showed substantial smoking of lettuce cigarettes when working for water reward (Block 1) but such smoking behavior was all but eliminated when water was given ad lib in the quasi-extinction sessions (Block 2). Smoking of cocaine cigarettes for water reward produced high puff rates as well as high puff durations (Block 3). When water was again given ad lib (Block 4), cocaine smoking was significantly reduced in 2 animals but remained significantly higher than lettuce quasi-extinction sessions. Indeed, Alex showed no significant change in puff frequency or duation when smoking cocaine cigarettes with water ad lib. During choice sessions, both Alex and Phoebe displayed a significant preference for cocaine cigarettes in terms of puff frequency. However, while Phoebe's mean puff duration on cocaine cigarettes was significantly higher than on lettuce cigarettes, Alex showed no change in this measure.

The distribution of responses also changed during cocaine sessions. During lettuce sessions (Block 1), monkeys responding for water usually puffed at a high rate at the beginning of a session. Presentation of the green light and water reward was characterized by an initial brief pause, followed by a steady rate of responding. Responding was gradually reduced as the session progressed. No substantial differences were observed over these daily lettuce sessions. Providing water ad lib (Block 2) resulted in irregular responding at greatly reduced rates and responding extinguished completely over sessions. During initial cocaine sessions, monkeys responding for water (Block 3) regularly maintained a high rate of responding throughout the entire session with only brief pauses during the green light. Responding over such sessions was marked by increasing pauses. When water was provided ad lib during cocaine sessions (Block 4), responding remained at high rates at the beginning of a session, followed by increasing pauses, and some disruption of the characteristic steady rate of responding as sessions continued.

It was also observed that the topography of the puff response changed in both these animals when responding on cocaine cigarettes. The normal long puff duration (average 1000 msec.) were reduced to short puff durations of approximately 500 msec. This could account for the finding that urinary excretion of benzoyl ecgonine did not increase dramatically with longer cumulative puff durations in pilot sessions (see Table 3). Thus, while appearing to self-administer cocaine cigarettes for no additional rewards

(Block 4), these animals may have been exhibiting an increase in response rate without concomitant increases in drug intake due to these shortened puff durations. Unfortunately urine assays, which are necessary for confirmation of this notion, were not conducted during these test blocks.

GENERAL DISCUSSION

The most apparent aspect of these findings is that monkeys will self-administer cocaine, albeit in small amounts, via chewing and smoking when provided with an experimental opportunity to do so.

When cocaine hydrochloride was placed in a gum vehicle, monkeys worked on a FR 10 schedule for delivery of gum and such performance was marked by increased ITI responding coupled with frequent pauses. These changes are particularly interesting given the relative insensitivity of FR schedules to drug effects. However, performance here was similar to that seen on FR-FI responding in pigeons treated with cocaine (10 mg/kg, IM) [19]. Similar FR pauses have been observed with cocaine self-administration in rats [7] and squirrel monkeys [12]. In addition, while cocaine gum was not consistently preferred by the monkeys in choice tests, food barks and allied vocalizations decreased dramatically in sessions where monkeys were responding for cocaine gum alone. While these vocalizations still appeared to be food calls, their observed decrease in frequency may reflect a concomitant decrease in the food reinforcement strength of cocaine gum. This notion is supported by our observations that the monkeys sometimes ignored for several hours, their food and fruit supplements in their home cages after the cocaine sessions. In addition, the animals appeared hyperactive and engaged in stereotypic behaviors similar to those seen following cocaine [27] or *d*-amphetamine administration [cf. 8]. Similar increases in activity and reductions in food intake were observed in rats when treated with 68.9–130.3 mg/kg cocaine hydrochloride on food [29]. Indeed, in a companion procedure, neither 72 hr of food deprivation nor 72 hr of food satiation resulted in significant changes in total daily cocaine gum intake. This latter result is in agreement with Wilson's [33] findings for IV cocaine self-administration in rhesus monkeys.

It is interesting to compare the choice tests in these chewing studies with those found in the intravenous studies. In general, on comparisons between drugs administered intravenously, the higher dose is generally preferred regardless of the drug [17] and the higher of 2 doses of cocaine is also preferred [16,18]. Indeed, the self-administration literature suggests that cocaine is perhaps one of the most effective reinforcers when given via the IV route. Nonetheless, in the present studies, both monkeys clearly preferred plain gum to cocaine gum (Table 2), suggesting that taste and local anesthetic effects may have been factors here. When such variables were controlled with procaine gum, the preferences were equivocal, raising the further question of speed of absorption as a critical determinant in reinforcement efficacy.

Indeed, when cocaine was administered via the more efficient and rapid inhalation route, by addition of cocaine base to lettuce cigarettes, all monkeys significantly preferred cocaine cigarettes to vehicle alone (Table 4). (While no known active placebo was used in these smoking choice tests, it is interesting to note that the *Lactuca sativa* vehicle contains lactucarine which has been credited with narcotic properties and used as both an opium substitute and a stimulant [31]. The smoking preference was indicated by increases in puff duration which did not always covary with frequency of puffs themselves. Since puff duration and not frequency was the more reliable indicator of drug intake and was correlated with urinary metabolite levels (Table 2), some caution must be applied in interpreting previous studies which used puff frequency alone in assessing smoking preferences of monkeys [10,30]. The smoking of cocaine cigarettes in the present study, which persisted even when water reinforcement was eliminated, was characterized by animals receiving fewer reinforcements (water) per session and having reduced puff durations (reduced efficiency). Such results are similar to the effects of Δ^9-tetrahydrocannabinol administered via smoking to great apes working for food reward [6]. The distribution of responses during cocaine smoking sessions was marked by initial high rates followed by increasing pauses over sessions or when water was provided ad lib. These latter results are similar to the effects of cocaine administered IV to squirrel monkeys working for food reward [12].

While more work is needed to fully understand the differences between cocaine self-administration via different routes, given limited daily access to cocaine gum, the monkeys in the present studies did self-administer the same amount daily regardless of food deprivation or food satiation. The latter result is in agreement with the effects of cocaine IV self-administration [32,33]. In addition, the total daily amount chewed by the monkeys was roughly equivalent to the total daily intake for human coca chewers (see Introduction). These findings coupled with the significant preference for cocaine cigarettes and maintenance of their self-administration through quasi-extinction sessions, suggests the potential application of these animal models for the study of human coca chewing and smoking, heretofore only anecdotally reported.

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