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Cocaine's effects on the discrimination of simple and complex auditory stimuli by baboons

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Abstract

The effects of cocaine on tone frequency discriminations by baboons were examined and compared with previous data for more complex acoustic stimuli (speech sounds) to see if cocaine's perceptual effects on these discriminations depends upon the type of stimulus employed (i.e., tones vs. speech sounds). Baboons pressed a lever to produce one repeating ''standard'' tone and released the lever only when one of four other ''comparison'' tones occasionally occurred in place of the standard tone. Cocaine's effects were assessed once or twice weekly by giving an intramuscular injection of cocaine hydrochloride (0.01–0.56 mg/kg) immediately prior to performing the task and by examining correct detections and reaction times for each tone following drug administration. Cocaine impaired tone discriminability, with greater impairments occurring for those tones that were more similar in frequency to the standard tone. Cocaine's perceptual effects occurred within 20–70 min following drug administration. Cocaine also impaired or facilitated the speed of responding to auditory stimuli, depending upon the drug dose and subject. The results demonstrate that cocaine can impair auditory discriminations involving simple tones, as well as speech sounds, and further supports the suggestion that cocaine's effects are focused on CNS mechanisms related to the use of pitch cues.

Keywords: Cocaine; Auditory perception; Discrimination; Baboon; Reaction time; Lever release

1. Introduction

Experimental evidence supports the claims of both improved and impaired performances following the administration of cocaine. In rats, cocaine has been reported to enhance accuracy in a vigilance task (Grilly and Grogan, 1990; Grilly and Nocjar, 1990), decrease response latencies (Grilly, 1992) and lower the threshold for the reinforcing effects of brain stimulation (Kornetsky and Esposito, 1981). On the other hand, cocaine has been shown to impair discriminative motor control in rats (Falk and Lau, 1991), elevate the threshold for the detection of brain stimulation in rats (Kornetsky and Esposito, 1981) and decrease the accuracy and rate of completing complex response sequences in monkeys (Branch and Sizemore, 1988). In humans as well, cocaine can impair accuracy in a repeated acquisition task (Fischman, 1984), but it can also increase Vigor and Arousal scores on the Profile of Mood States (POMS) inventory (Foltin and Fischman, 1991), improve performance accuracy on a digit symbol substitution test (Higgins et al., 1990) and improve reaction time speed on a visual attention task (Stillman et al., 1993). Such diverse results suggest that cocaine likely affects an array of biological and behavioral mechanisms underlying the performances in question.

Prior research from this laboratory has been elucidating the conditions under which cocaine may either enhance or impair perceptual/motor function and has demonstrated that cocaine can simultaneously improve some aspects of a behavioral performance while impairing others. Thus, cocaine can enhance motor function by shortening reaction times to simple tones in a detection task and to speech sounds in a discrimination task (Hienz et al., 1993, 1994, 1995). At the same time, cocaine can impair perceptual function by reducing accuracy in the discrimination of

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speech sounds, but not in the detection of tones (Hienz et al., 1995). These results suggest that cocaine's perceptual effects on these discriminations may depend upon either the type of stimulus employed (i.e., tones vs. speech sounds) or the procedure (i.e., detection vs. discrimination). The present report extends these studies by using a discrimination procedure to assess the effects of cocaine on simple tone discriminability. Baboons were trained to press and hold a lever down and to release the lever only when a change in tone pitch occurred (i.e., from one tone pitch to another). The effects of cocaine on tone discrimination accuracy are contrasted with the data of previous studies in which in baboons discriminated among human vowel sounds of similar pitch (Hienz et al., 1995). Additionally, reaction times to the stimuli were measured to assess whether cocaine had similar motor effects to those previously reported (Hienz et al., 1993, 1995).

2. Method

2.1. Subjects

Three adult male baboons (*Papio anubis*) weighing between 25 and 33 kg served as subjects. These were the same baboons employed in a previous study of the effects of cocaine and quinpirole on the discrimination of speech sounds (Hienz et al., 1997). Each baboon was housed separately in a large-primate cage equipped with a seating bench. All animals had auditory and visual contact with other baboons housed in the same colony room. The animals were maintained on a 22-h restricted feeding schedule with water continuously available in the home cage. Supplemental monkey chow and two pieces of fresh fruit were provided daily after each experimental session. The baboons were maintained on a daily 12-h light/dark cycle (6 a.m./6 p.m.). The experimental protocol for these studies was approved by an Institutional Review Committee for the use of animal subjects, and the procedures were in compliance with the National Institutes of Health Guide for Care and Use of Laboratory Animals.

2.2. Apparatus

The test cage was a modified primate squeeze cage placed inside a double-walled, sound-attenuating chamber (IAC, Model 1201A). A 76-cm-wide by 97-cm-high intelligence panel was attached to one side of the test cage and contained a red light-emitting diode as a cue light, a feeder opening for delivery of 500-mg banana-flavored pellets and a primate lever (BRS/LVE Model PRL-003). With a baboon seated on a metal bench facing the panel, the cue light was at eye level, the feeder opening 25 cm below the cue light and the response lever at waist level in front of the right arm. Each baboon was moved from his home cage to the test cage via a metal transfer cage. Stimulus presentations, response measures and contingencies were controlled by Apple IIe computers.

2.3. Stimuli

The tone frequencies employed were 1025 Hz as the standard tone frequency, and 1225, 1510, 1668 and 1736 Hz as the comparison tone frequencies. These frequencies were chosen to approximate the second formant (F_2) frequencies of the vowels employed in our previous studies (e.g., Hienz et al., 1995); F_2 frequencies were used as the basis for this selection because first formant (F_1) frequencies often do not differ significantly from one another (e.g., the synthetic vowels /a/ and /æ/ have identical F_1's), and previous results indicated that drug effects on vowel discriminations are most frequently correlated with changes in F_2 (Hienz and Brady, 1988). All acoustic signals were generated by a Coulbourn Instruments oscillator and then passed through an electronic switch (20 ms rise/fall times) to eliminate possible clicks, and then to a programmable attenuator and amplifier. The system was calibrated with a General Radio sound level meter, a Bruel and Kjaer amplifier and a 1.25-cm condenser microphone located at ear level facing the speaker. Signals were passed to a wide-range speaker in each test chamber, which was located 20 cm above the ear level of a baboon's head as he sat inside the test cage. All stimuli were 120 ms in duration, were presented at a rate of 2/s and had an average intensity of 75 dB sound pressure level (SPL). To prevent subjects from responding to any possible differences in intensity among stimuli, stimulus intensity was varied randomly (± 3 dB) prior to each stimulus presentation.

2.4. Procedure

A discrete-trial procedure was employed in which baboons were trained to hold down the lever to produce a series of repeating pulses of a standard tone frequency (e.g., "Tone-A"–"Tone-A"–"Tone-A"–"Tone-A"–"Tone-A", etc.) and to release the lever only when a different or "comparison" tone frequency began alternating with the standard tone (e.g., "Tone-A"–"Tone-A"–"Tone-A"–"*Tone-B*"–"Tone-A"–"*Tone-B*", etc.). The flashing red cue light (5/s) signaled the start of each trial. Once the lever was pressed, the cue light became steady, and the train of standard tone pulses (2/s) began. One of the four comparison tone frequencies was randomly selected to alternate with the standard tone on each trial. This stimulus change between the standard and the selected comparison tone began at a random time of between 1 and 7 s following the initial lever press. Two presentations of the comparison tone alternated with the standard tone (e.g., "Tone-A"–"Tone-A"–"Tone-A"–"*Tone-B*"–"Tone-A"–"*Tone-B*"). This resulted in a stimulus alternation interval 1.5 s in duration, as measured from the onset of the first comparison tone. Release of the lever at any time within this 1.5-s

interval was reinforced with a banana-flavored pellet, following which all stimuli were terminated. A 4-s intertrial interval (ITI) followed, and any lever responses during the ITI reinitiated the ITI. Lever releases in the absence of stimulus changes produced an 11- to 15-s timeout from the contingencies, signaled by terminating the cue light. Failure to detect the stimulus change, as indicated by holding the lever through the 1.5 s of the alternation period, resulted in the termination of all stimuli; the light remained off until the lever was released, following which the next ITI was initiated. Randomly on 20% of the trials, ''catch'' trials were presented to measure false-alarm rates; during each catch trial the standard tone alternated with itself throughout the trial. Lever releases during catch trials also produced a timeout of 11–15 s.

2.5. Data collection and analysis

Sessions were 100 min in duration and occurred 5 days a week at approximately the same time each day. Each session was divided into blocks of 100 trials each. During a session, baboons typically performed five full blocks of trials, i.e., 500 discrimination trials. For each comparison stimulus, the percent correct score for each block of trials was defined as the number of releases within the 1.5-s alternation interval divided by the total number of trials presented for each comparison stimulus within the block, multiplied by 100. False alarm rates were defined as the number of releases within the 1.5-s alternation interval when no stimulus change occurred, divided by the total number of catch trials presented within the block, multiplied by 100. Reaction times to each comparison stimulus were timed from the onset of the first presentation of a comparison stimulus to the release of the lever. For correct releases only, median reaction times to each comparison stimulus were computed for each block of trials; medians of the reaction times were calculated because the physiological limits on reaction times can skew reaction time distributions. Baseline performances were defined as stable when the following conditions were met: (1) percentage correct responses to all comparison stimuli were 80% or greater during all blocks in a session; (2) false-alarm rates were less than 30% for all blocks of trials in a session; (3) median reaction times for each block of trials in a session were within 50 ms of one another; and (4) there were no systematic changes in the time course of these measures across blocks within a session or across sessions. Because cocaine reduced both percent correct scores and reaction times, the ''maximal effect'' of cocaine on these measures was calculated by selecting the lowest percent correct score and median reaction time value from among the four to five blocks of trials of each drug session, and subtracting from them the mean of the corresponding measures from the preceding day's saline control session. For comparison, estimates for percent correct scores and reaction times following vehicle (saline) injections were calculated in an identical manner.

2.6. Drug administration

Cocaine and saline were administered intramuscularly in the gluteal region. Injections were given at approximately the same time each day, immediately before the session and after each baboon had been transferred to the test chamber. The actual injection site was varied from day to day to avoid tissue damage from frequent injections. Cocaine doses were administered once or twice weekly, typically on Tuesdays and/or Fridays. On nondrug days, 0.5 ml NaCl vehicle was injected. All drug volumes were adjusted to be about 0.5 ml, with concentrations derived by dissolving drug in appropriate vehicle (0.9% sterile saline). Cocaine doses administered ranged from 0.01 to 1.0 mg/kg. The dose range included doses that produced cessation of responding. Each dose was administered at least twice in mixed order, and additional doses were administered if there were large differences between first and second exposures at a dose.

3. Results

Baseline discrimination performances of all three baboons were maintained at a high level. Fig. 1 shows each of the baboons' present discrimination performances, along with data from their previous discrimination performances with vowels for comparison. Each bar represents the average performance for each stimulus type across the first 10 saline sessions of each study. All baboons performed at the near-100% level for all four vowels and for the three higher-frequency tones, with performances dropping slightly to an average of 93% for the fourth tone. Baseline false alarm rates were also comparable for both types of stimuli. The acquisition data of all baboons was also examined for correlations between discrimination accuracy for the different stimuli and the number of days until performances stabilized, but no significant correlations were found.

Fig. 2 (left) shows the dose-related effects of cocaine on the discriminability of each of the four comparison tones averaged across baboons. Also shown are average data on cocaine's effects on the discriminability of vowels with comparable F_2 changes for the same baboons (Fig. 2, right), based upon the data of Hienz et al. (1995). The same symbols are used in each graph for stimuli that approximate one another in terms of the tone pitch changes (left graph) and second formant vowel changes (right graph). For the first three stimuli, differences between the effects of cocaine on tone discriminations and vowel discriminations were minimal when the decreases in percent correct scores are examined relative to the 95% confidence limits and over comparable doses. For the 4th stimulus, however, greater reductions in discrimination performances were observed following cocaine for the tone stimulus than the vowel stimulus. None of the baboons showed significant changes in false alarm rates following for either tones or vowels (data not shown).

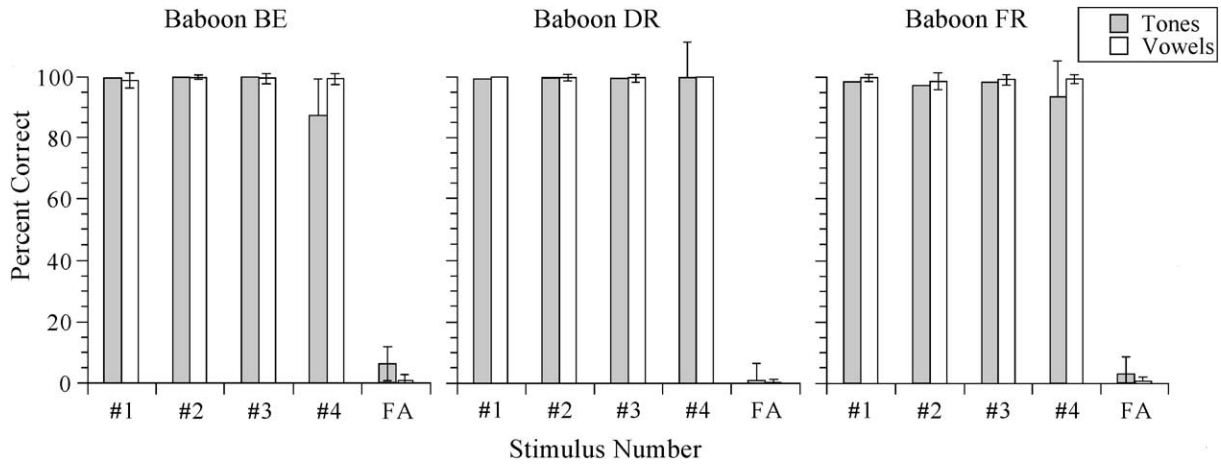

Fig. 1. Baseline discrimination performances of each baboon, showing the percentage of correct detections of the indicated four tones and vowels (nos. 1–4), and false alarm (FA) rates. Error bars represent ±1 S.D. Pitches for tones 1–4 were 1736, 1668, 1510 and 1225 Hz, respectively. F_2 frequencies for vowels 1–4 were 1724, 1674, 1319 and 1237 Hz (as taken from the vowels /æ/, /ɛ/, /u/ and /a/, respectively). Thus, each set of columns in each graph are for stimuli that approximate one another in terms of the tone pitch changes and second formant vowel changes.

A detailed comparison of the individual performances for the three baboons is shown in Fig. 3 for the tone most affected (1225 Hz), and the vowel /a/, which was strongly affected in two of three baboons in the prior study (Hienz et al., 1995). Cocaine produced comparable decreases in the accuracy in detecting the tone and vowel changes in Baboon BE. Cocaine had no effect on Baboon DR's prior vowel discrimination performance, but it did produce a small effect on his tone discrimination performance. Finally, cocaine had a greater effect on Baboon FR's tone discrimination performance than on his prior vowel discrimination performance. Thus, cocaine's effects on tone discrimination performances were either comparable to or greater than cocaine's previously documented effects on vowel discrimination performances.

Fig. 4 shows the changes in tone discriminability as a function of the differences in tone frequency between the comparison and standard stimuli. Each data point is for the cocaine dose most effective in reducing tone discriminability for each baboon (0.32, 0.1 and 0.56 mg/kg, respectively, for Baboons BE, DR and FR). Two of the three baboons, BE and FR, showed clear frequency-related effects on tone discriminability following cocaine, whereas Baboon DR did not, partly due to the small size of cocaine's effects on his performance.

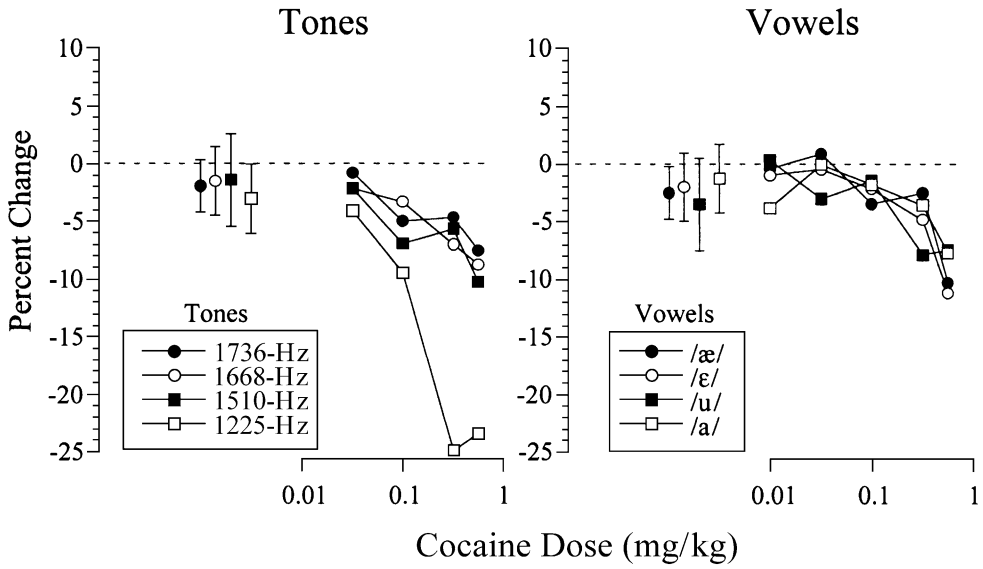

Fig. 2. Average changes in tone (left) and vowel (right) discriminability as a function of cocaine drug dose for each of the indicated four stimuli. The same symbols are used in each graph for stimuli that approximate one another in terms of the tone pitch changes (left graph) and second formant vowel changes (right graph). Error bars encompass 95% confidence limits about the saline/vehicle points.

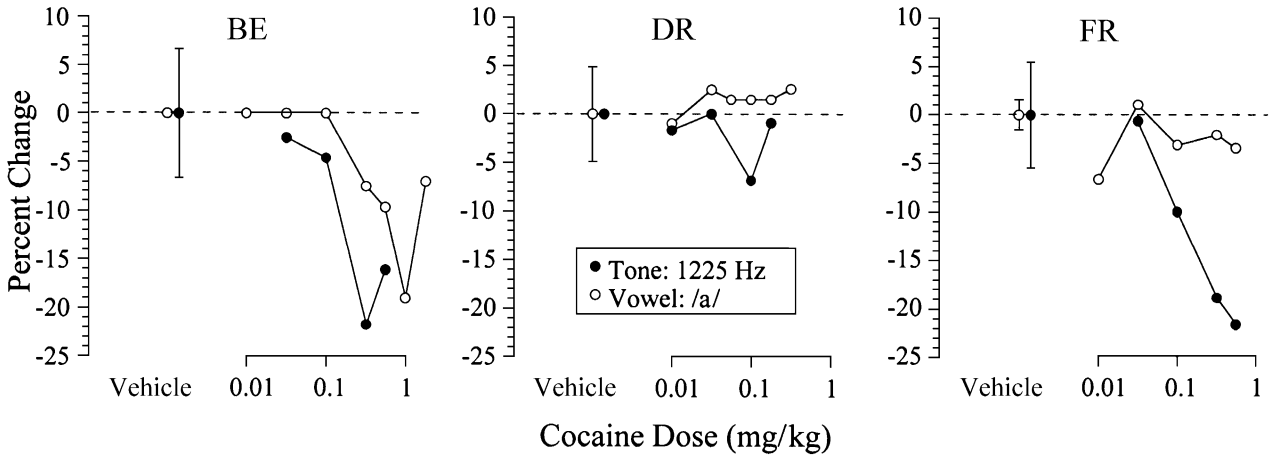

Fig. 3. Changes in stimulus discriminability at the time of peak drug effect for the 1225-Hz tone (filled symbols) and the vowel /a/ (open symbols), plotted as a function of drug dose. Error bars encompass 95% confidence limits about the vehicle points. Vehicle control data were derived in an identical manner.

The maximally effective doses of cocaine typically produced decrements in discriminability within the first 20–30 min of a session, which were then maintained at this reduced level until about 50–70 min into a session. At the highest drug doses tested, pauses in performances often occurred. When pausing occurred, baboons typically responded during the first 10–20 min of a session, stopped responding until about 50–70 min into the session and thereafter resumed responding sporadically. The data obtained at these high doses were included for completeness, but they only indicate the effects of cocaine on discriminability relatively early within a session. Occasional upturns in the dose–effect functions at the high doses thus likely reflect this early cessation of responding during a session. Finally, the observed decreases in discriminability produced by cocaine did not change over the course of the study—that is, for those baboons and doses showing decrements in discriminability, both the first and second exposures at a given dose produced effects of similar magnitude.

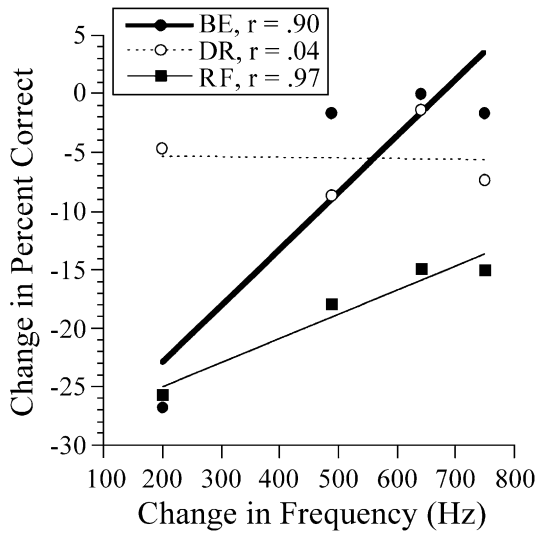

Fig. 4. Changes in tone discriminability as a function of the differences in tone frequency between the comparison and standard stimuli. Each data point is for the cocaine dose most effective in reducing tone discriminability for each baboon; doses selected were 0.32, 0.1 and 0.56 mg/kg, respectively, for Baboons BE, DR and FR.

Fig. 5 shows the dose-related effects of cocaine on reaction times for each baboon. The data shown are averages across all comparison vowels or tones, since no significant differences in reaction times were observed among the different tone or vowel stimuli in the presence or absence of drug. Fig. 5 shows the "maximal effect" changes in reaction times averaged across the stimuli as a function of drug dose for each baboon for tones (filled symbols) and vowels (open symbols). As in previous studies (Hienz et al., 1993, 1994), cocaine shortened reaction times for vowels, an effect that occurred for all baboons at some dose. For Baboons BE and FR, reaction times returned to or were slightly lengthened above baseline levels at the higher doses; Baboon DR's vowel reaction times were shortened up to a cocaine dose of 0.18 mg/kg; repeated administrations at a slightly higher dose of 0.32 mg/kg produced cessation of responding in this baboon. For tones, cocaine similarly shortened reaction times for Baboon BE across most of the dose range in which he responded. Baboon FR showed shortened reaction times following the lowest cocaine dose but markedly lengthened reaction times at the higher doses. Baboon DR, on the other hand, showed lengthened reaction times to the tones following cocaine. This difference in Baboon DR's reaction time changes for tones and vowels was possibly due to a "floor" effect on the baseline reaction time performance with tones. Average nondrug reaction times to vowels ranged from 550 to 580 msec for all three baboons, while average nondrug reaction times to tones were 400 msec for Baboon DR, 435 msec for Baboon BE and 555 msec for Baboon FR. Thus, Baboon DR exhibited

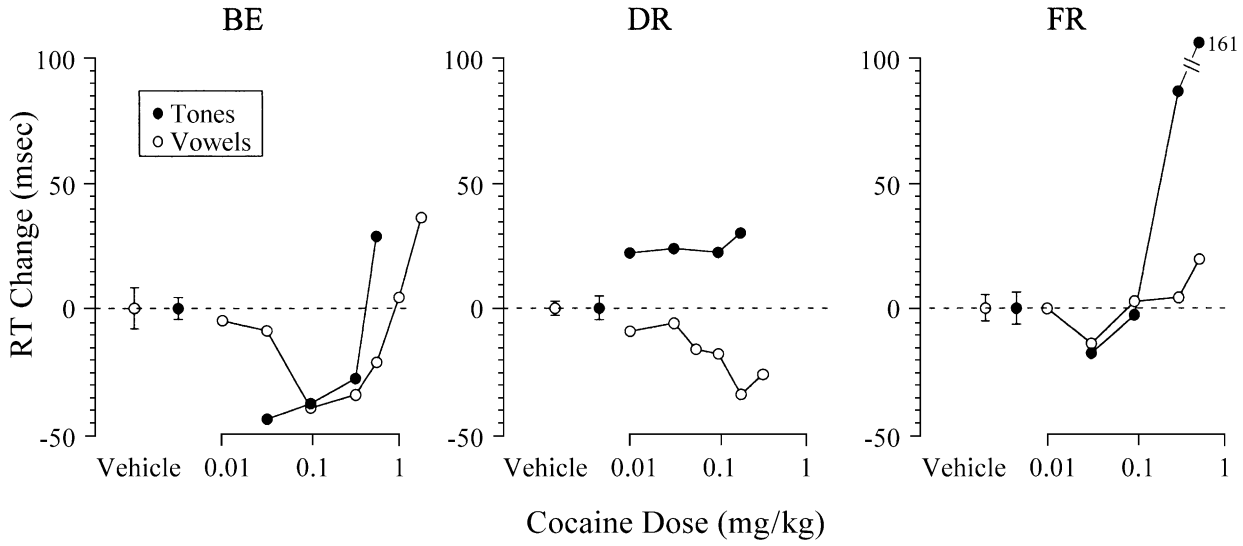

Fig. 5. Changes in reaction times at the time of peak drug effect for tones (filled symbols) and vowels (open symbols), plotted as a function of drug dose. Error bars encompass 95% confidence limits about the vehicle points. Vehicle control data were derived in an identical manner.

the shortest tone reaction times of all and evidenced slightly elevated tone reaction times following cocaine.

The drug-induced changes in reaction times followed a similar time course of change to those observed for percent correct scores in that cocaine produced a general (increasing/decreasing) trend in reaction times throughout a session. As noted previously, baboons stopped responding about 20–30 min into a session at the highest doses tested. Such behavioral disruptions may be responsible in part for the upturns in dose–effect functions seen in Fig. 5. The reaction time changes produced by cocaine did not change over the course of the study—both the first and second exposures at a given dose produced effects of similar magnitude for those baboon/dose combinations showing significant changes in reaction times.

4. Discussion

The results of the present study show that cocaine can impair the discriminability of tone pitches in baboons and can concurrently affect the speed of responding to the tone stimuli. Previous reports have described either facilitative or decremental effects of cocaine on behavioral performances that appear to depend on the type of performance being examined. For example, the performances of rats on vigilance tasks are facilitated following cocaine (Grilly and Grogan, 1990; Grilly and Nocjar, 1990), while the accuracy of completing chains of complex response sequences in monkeys are impaired following cocaine (Branch and Sizemore, 1988). Obviously, such differences in cocaine's effects on different behavioral performances may be a function of a number of variables including such things as drug dose, species employed and behavioral procedures employed. On the other hand, the present study describes both facilitative and decremental effects of cocaine within the same procedure and subjects, and it also replicates previous findings of similar effects of cocaine on these same performance measures when baboons were discriminating among different human vowel sounds (Hienz et al., 1995). Thus, cocaine can simultaneously evidence distinctly different effects (i.e., facilitative and decremental) on different aspects of a single behavioral performance.

No evidence was found for an "enhancing" effect of cocaine upon discrimination accuracy. While such enhancements have been reported by others (e.g., Grilly and Grogan, 1990; Grilly and Nocjar, 1990), many differences in species and procedures could account for this lack of enhancement on accuracy in the present procedure. Additionally, baseline discrimination accuracy levels were high in the present study so that a ceiling effect could have been present on accuracy changes for the more easily discriminated stimuli. On the other hand, the effects of cocaine on vowel discriminations have also been examined in the presence of background noise that was titrated up and down to produce differing levels of baseline performance accuracy (e.g., high, medium and low discriminability of the stimuli in noise; Hienz et al., 2001). When baseline performances were degraded under these conditions, cocaine still did not enhance discrimination accuracy; on the contrary, cocaine's decremental effects on discrimination accuracy were greatly magnified when the baseline was slightly degraded under the low-noise condition, compared to the no-noise condition, and more severely degraded performances under medium- and high-noise conditions. It thus seems unlikely that a ceiling effect in the present study accounted for the lack of any enhancement of the discrimination accuracy performances.

Previous results have shown that stimulus discriminability is impaired following cocaine in a speech discrimination task, but stimulus detectability is not in a tone detection task

(Hienz et al., 1995). These results suggest that cocaine's effects on these discriminations may have been dependent upon either the type of stimulus employed (tones vs. speech sounds) and/or the type of procedure employed (i.e., detection vs. discrimination). The present demonstration of cocaine's effects on tone pitch discriminations suggests that the lack of an effect of cocaine on the detectability of tones may be related more to the existing procedural differences than the stimulus differences between these studies. In the tone detection procedure, baboons performed a reaction time task in which they were trained to press and hold a lever and to release it only after the occurrence of a near-threshold tone (Hienz et al., 1993, 1994). In the stimulus discrimination procedures, however, baboons were trained to respond to a stimulus change from one sound to another (e.g., from one vowel sound to a different vowel sound, or from one tone pitch to a different tone pitch), as opposed to simply detecting the presence or absence of an acoustic stimulus. It is under this condition of discriminating a stimulus change that decrements in discriminability are observed following cocaine, for both simple tones and for more acoustically complex human vowel sounds.

As seen in Fig. 2, cocaine produced a much greater impairment for the discrimination of the 1225-Hz tone than for any of the previously tested vowel stimuli. Such a result is not surprising, given the differences in the acoustic structures of the present tones and vowels. The discrimination of the 1225-Hz tone would require an animal to detect a 200-Hz change in pitch from the standard tone of 1025 Hz. On the other hand, all the vowel stimuli have much more complex spectral shapes consisting of multiple resonances, or "formants" (e.g., F_1, F_2, F_3, etc.), which can contribute to the discrimination of one vowel from another. The "worst-case" vowel discrimination for the present study was between the comparison vowel /a/ ("ah") and the standard vowel /ç/ ("aw"). Discrimination between these two stimuli would require an animal to detect either a 200-Hz change in F_2 pitch, or a 56-Hz change in F_1 pitch, or changes in the amplitudes of either F_2 or F_1, as well as multiple combinations of these different cues. Thus, the wide variety in cues between natural vowels could make these discrimination less likely to be affected following administrations of cocaine.

The present results also lend further support to previous suggestions of the nature of cocaine's effects being focused upon mechanisms involved in the processing of acoustic pitch cues, rather than other cues such as loudness or duration. As previously noted, cocaine does not affect behavioral thresholds for the detection of pure tones, but does so for the detection of light intensity (Hienz et al., 1993, 1994), and thus is modality specific in affecting stimulus detectability. Additionally, similar reductions in human event-related potentials following cocaine have been reported in an "oddball" task in which humans detect infrequently presented tones of differing frequencies (Robledo et al., 1993). Further, reductions in vowel discriminability following cocaine are greater for those vowels in which the acoustic frequency differences (i.e., "formant" differences) between standard and target vowels are smaller (Hienz et al., 1995). Thus, cocaine reduces vowel discriminability moreso when vowels are more similar in terms of their acoustic structure. Previous reports of diazepam's effects on vowel discriminability (Hienz and Brady, 1987, 1988, 1989) have described similar relationships among formant differences and diazepam's effects upon vowel discriminations. The results of the present study also showed such a correlation between the cocaine-induced reductions in tone discriminability and the differences in pitch between the comparison and standard tones for two of the three baboons. Taken together, these results suggest cocaine's likely influence on central nervous system (CNS) mechanisms related to the use of pitch cues involved in the processing of acoustic stimuli. Additionally, the threshold detection task employed in past studies appears to be the most difficult to learn, and the vowel and tone discriminations were more quickly acquired (Hienz and Brady, 1988); yet, the latter discriminations are much more affected by drugs such as cocaine.

In the present study, cocaine shortened reaction times for two of the three baboons over some part of the dose range. The third baboon showed consistently longer reaction times following cocaine, but had previously shown consistently shorter reaction times following cocaine for vowel stimuli. One possible explanation for this discrepancy is that the marked differences in this baboon's baseline reaction times for tones and vowels (400 vs. 550 msec) resulted in a floor effect that prohibited further reaction time decreases. This baseline difference would not, however, appear to account for cocaine's increasing tone reaction times for this baboon. Thus, it is not clear at the present time what variables influence the direction in which cocaine affects reaction times. In an earlier study, acute cocaine administered once or twice weekly shortened reaction times in a tone detection task for all six of the baboons studied (Hienz et al., 1993). In a similar study, chronically administered cocaine shortened reaction times in two baboons and lengthened reaction times in the remaining two baboons (Hienz et al., 1994). In neither of these studies was the direction of the RT effect found to be time dependent within sessions. On the other hand, in two studies of cocaine's acute effects on reaction times to speech sounds (Hienz et al., 1995, 1997), cocaine shortened reaction times in only four of the six baboons studied. Additionally, a prior study of the effects of D-methamphetamine on reaction times in baboons also found that D-methamphetamine shortened reaction times in some baboons and lengthened reaction times in others (Hienz et al., 1985), depending upon the dose and subject. In these studies, no relationships were found between drug history and the direction of cocaine's effect upon reaction time. Additionally, for D-methamphetamine, no relationship was found between baseline reaction time values and the direction of the drug effect.

A number of dopaminergic (DA) pharmacological investigations have strongly implicated the DA system as a mediator of reaction time performances. The majority of these studies have been performed in rodents, although the effects of indirect DA agonists on reaction time also have been tested in baboons. For instance, both systemic administration of the indirect DA agonist D-amphetamine and intrastriatal administration of DA itself have been shown to decrease response latencies in rats trained to release a lever within 0.7 s of the onset of a stimulus light (Baunez et al., 1995); both compounds also produced overall performance impairments by increasing premature lever releases. Decreases in response latency following D-amphetamine administration have been reported in a similar lever-release paradigm maintained by shock avoidance (Mayfield et al., 1993). In rhesus monkeys, DA antagonists such as SCH 39166 and raclopride have been shown to produce dose-dependent slowing of reaction times, while D-amphetamine has more inconsistent effects in that it may either increase or decrease reaction times, depending upon the animal and drug dose (Weed and Gold, 1998). In baboons, mo-derately high doses of the indirect DA agonists cocaine or D-methamphetamine can decrease response latencies to either visual or auditory stimuli without the large impairments in accuracy of responding typically seen in rodent studies (Hienz et al., 1985, 1993, 1994, 1995). These studies in baboons typically show ''U'' shaped dose–response functions where moderately high doses that decrease latencies are followed by higher doses that increase response latencies back to and often above baseline levels. These effects show marked inter-animal variation for indirect DA agonists (Hienz et al., 1985, 1993, 1994, 1995). On the other hand, the D_2-like agonist quinpirole has been shown to produce dose-dependent *increases* in reaction time performances in baboons (Hienz et al., 1997). These opposite effects of cocaine and quinpirole on reaction times in baboons are at odds with the previously reported similarities of these two compounds for increasing motor activity in rats (Hooks et al., 1994; Scheel-Kruger et al., 1977) and increasing response rates for schedule-controlled behavior in squirrel monkeys (Barrett, 1974; Katz and Witkin, 1993; Witkin et al., 1991). Such contrasting effects of cocaine and quinpirole could be due to the fact that the changes in reaction times under these two compounds may not be mediated solely by DA activity, but also by other non-DA mechanisms as well. Additionally, it becomes difficult to generalize the effects of these compounds on behavior across different species.

In conclusion, the present results show that cocaine can impair auditory perceptual discriminations based upon differences in tone pitch in baboons, and thus parallel previous findings of impairments in the discrimination of human vowel sounds following cocaine in baboons (Hienz et al., 1995). These results suggest that cocaine may adversely affect CNS mechanisms involved in the analysis or use of acoustic pitch cues. Additionally, cocaine can facilitate or impair the speed of responding to auditory stimuli, depending upon the drug dose and subject.

Acknowledgments

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