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Effects of Cocaine on Sensory Motor Function in Baboons

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HIENZ, R. D., D. J. SPEAR, J. V. BRADY AND D. A. BOWERS. *Effects of cocaine on sensory motor function in baboons.* PHARMACOL BIOCHEM BEHAV 45(2) 399–408, 1993.—The effects of cocaine on auditory and visual threshold functions and reaction times were studied in baboons. Single IM injections of cocaine HCl (0.001–1.0 mg/kg) were administered once or twice weekly and were followed immediately by psychophysical tests designed to assess cocaine's effects on sensory thresholds and reaction times. Consistent reductions in reaction times were observed in the cocaine dose range of 0.032–0.32 mg/kg. Reaction times were decreased by 5–8% at the more effective cocaine doses. Concurrently measured auditory and visual threshold sensitivities showed no systematic changes at any of the cocaine doses studied.

Cocaine Reaction time Threshold Psychophysical procedure Lever press Baboon

THE view that cocaine can enhance human performance is widespread. Anecdotal reports by cocaine users and chewers describe enhancement of performance attributed to such drug use, but these effects have rarely been tested experimentally (3). Cocaine has recently been shown to increase vigor and arousal scores on the Profile of Mood States (POMS) inventory in humans (5) and improve human performance on a digit symbol substitution test (12). Only limited experimental data exist on the effects of cocaine on simple motor performances, and those few studies examining cocaine's effects in humans have not supported these subjective reports of enhanced abilities (3,13). For example, cocaine has no effect on hand-grip strength at IV or intranasal doses of 10 or 25 mg (22) and no effect on reaction times in rested subjects given 96 mg intranasally (4). When subjects are deprived of sleep, on the other hand, cocaine does reverse the deprivation-induced decrements in reaction times (4). This effect of cocaine parallels that reported for amphetamines, which appear to have minimal effects on humans under normal conditions but have been reported to return fatigue-induced performance decrements to normal levels (16,26). There is some evidence suggesting that cocaine may enhance some performances in nonhuman animals as well. For example, cocaine increases operant response rates of many species under many reinforcement schedules (6). Further, stimulants are also known to increase the frequency of general motor behavior in animals, especially repetitive, stereotypic movements (1,15,18,23).

One study has shown that the stimulant *d*-methamphetamine can significantly shorten reaction times in baboons performing an animal psychophysical procedure (11). These animals were trained in a "reaction time" procedure in which they pressed a lever when a "ready" signal occurred and released the lever when the reaction time stimulus occurred randomly in time after the ready signal. Reaction times to auditory stimuli progressively shortened with increasing *d*-methamphetamine dose, while concurrently obtained estimates of the baboons' hearing thresholds showed no change. Similar tests with visual stimuli also showed shortened reaction times accompanied by an elevation in visual threshold following *d*-methamphetamine, a noteworthy effect because a loss in sensitivity to visual stimuli might normally be expected to result in longer reaction times. The present study reports on the effects of single injections of cocaine given once or twice weekly on the performances of baboons in a reaction-time procedure and describes cocaine's effects on response latencies to auditory and visual stimuli, as well as on concurrently determined auditory and visual thresholds.

METHOD

Subjects

Subjects were six adult, male dog-faced baboons (*Papio cynocephalus*, cynocephalus and anubis types, supplied by Primate Imports) weighing between 18 and 26 kg. All subjects

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had previous experience with the experimental procedures. Three baboons (ER, ME, and MU) had extensive drug histories, including exposures to Δ^9-tetrahydrocannabinol (THC) and opiates; the remaining baboons (AC, BE, and CA) were drug naive except for once-monthly sedation with ketamine for physical examinations. Animals were housed in individual cages equipped with dripless water spouts. All animals were maintained on a 22-h restricted feeding schedule with supplemental monkey chow and fresh fruit provided on a daily basis immediately after each experimental session. The feeding schedule permitted progressive weight gain, although at 5–10% below ad lib weights. The general health and appearance of each animal was checked daily. Detailed medical examinations, including weight checks, were conducted monthly by trained and certified animal technicians. Animal care was in accordance with state and federal regulations governing the care and treatment of laboratory animals.

Apparatus

The testing apparatus consisted of a modified baboon squeeze cage fitted within a double-walled sound-attenuating chamber (Industrial Acoustics, Model 1201-A). A 76 × 97-cm "intelligence panel" attached to one side of the cage contained a primate lever (BRS/LVE Model PRL-003), a red light-emitting diode used as a cue light, a 2.5-cm diameter opaque Plexiglas visual stimulus patch, and a metal food hopper for delivery of 500-mg banana pellets. With a baboon positioned facing the panel, the cue light was at eye level and the response lever was at waist level in front of the right arm. With an animal sitting in the test cage and orienting toward the cue light, the visual angle between the cue light and the visual stimulus patch was approximately 15°. Acoustic signals were delivered by a wide-range speaker suspended outside the cage and located directly over the animal's head approximately 20 cm above ear level. Animals were moved from their home cages to the testing chamber via a metal transfer cage. Baboons were observed via a closed-circuit infrared TV monitoring system during test sessions.

Stimuli

Acoustic signals were 16.0-kHz pure tones that were generated by a Krohn-Hite oscillator and then passed through an electronic switch (20-ms rise/fall times), programmable attenuator, amplifier, and a wide-range speaker. 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. The light source for the visual stimuli was a slide projector that was mounted on the outside of the chamber and projected white light onto the back of the stimulus patch through an otherwise light-tight aperture in the chamber wall. Stimulus intensity was varied by using neutral density filters in the slide projector. Light intensities were calibrated with a light meter (United Detector Technology, Model 40X). Programming of the experiments and data collection were accomplished with an Apple IIe computer.

Procedure

Reaction times and sensory thresholds were measured using a self-paced reaction time procedure. Baboons initiated each of a series of discrete reaction time trials by pressing and holding down a lever when a ready signal was presented and releasing the lever only when the reaction time stimulus occurred. Details of the procedure were as follows: In the presence of the flashing red cue light (5/s), a lever press changed the flashing light to a steady light, which remained steady as feedback as long as the lever was held down. At intervals ranging from 1.0–7.0 s after initiation of this maintained holding response, a stimulus (white light on the circular patch during visual threshold testing or tone burst through the speaker during auditory threshold testing) was presented for 1.5 s. Release of the lever within the 1.5-s stimulus interval was reinforced with the delivery of one 500-mg banana-flavored pellet, followed by initiation of a 3-s intertrial interval (ITI), during which no stimuli were presented and lever responses reinitiated the ITI. Early lever releases prior to stimulus onset produced a 3-s timeout, then reinstated the 3-s ITI without reinforcement. If an animal failed to release the lever during a stimulus, the red cue light was turned off following stimulus offset and lever release then returned the animal to the ITI. Following the ITI, the flashing red cue light signaled initiation of the next trial in the series of several hundred trials in each daily 2-h experimental session. Baboons AC, BE, and ME performed the auditory reaction time procedure and baboons CA, ER, and MU performed the visual reaction time procedure. Baboons were also observed via the infrared camera system. On nondrug days, subjects were observed randomly for short periods of time during sessions. On drug days, subjects were generally observed during the 15-min dark adaptation period following drug injection and during the subsequent warm-up period and/or during lengthy pauses in responding. During auditory threshold testing sessions, such observations were not possible when animals were performing because high-frequency noise from the videocamera interfered with the detection of near-threshold tones.

Reaction Time and Threshold Determinations

Both auditory and visual reaction times and thresholds were determined by randomly varying the intensity of the stimuli from trial to trial (method of constant stimuli) and examining lever release latencies (i.e., reaction times) and detection frequencies (i.e., percent correct lever releases) at each intensity. Correct detections were defined as lever releases within 1.5 s of stimulus onset. A latency criterion for defining correct detections produces threshold estimates comparable to other psychophysical procedures if the latency criterion is 1 s or greater (21). For the auditory modality, four intensity levels (10 dB apart) of the 16.0-kHz pure tone were used, with the lowest level set just below an animal's estimated threshold. For the visual modality, four intensity levels (5 dB apart) of white light were used, with the lowest level set just below the animal's estimated threshold. By standard convention, tone intensities are specified in terms of dB sound pressure level (SPL); for comparative purposes, light intensities are specified in terms of a corresponding decibel scale of light intensity relative to an energy level of 0.000001 milliLamberts (which approximates the human threshold for scotopic vision). The difference in step size for auditory vs. visual stimuli is due to the use of pressure vs. energy scales for auditory and visual stimuli, respectively. To measure the false alarm or "guessing" rate of animals, a series of "catch" trials were randomly interspersed ($p = 0.20$) among both the auditory and visual test trials. During catch trials, no auditory or visual test stimuli were actually presented. Lever releases during catch trials produced a 3-s timeout.

Both auditory and visual test sessions occurred in a completely darkened experimental chamber, with normal testing starting after a 15-min dark adaptation period for each baboon (the cue light used to signal trial initiations was a small,

dim red light that did not appreciably affect dark adaptation). Test sessions were approximately 2 h long and were conducted 5 days/week, with each test session divided into blocks of 80–100 trials and each of the four intensity levels plus catch trials presented randomly approximately 20 times during each block. Each block of trials required about 15–20 min to complete, depending upon the animal. The first block of 80–100 trials after the 15-min adaptation period was considered a "warmup" block, and these data were not included in the standard analyses. Thus, the data for the present analyses were collected beginning 30–35 min after the start of each session. Four to five subsequent blocks of trials occurred within each session to provide a number of independent within-session estimates of the sensory thresholds and functions relating reaction time to intensity. Sensory thresholds were determined from the percentage of correct detections at each intensity by interpolating to the intensity that produced a detection score halfway between the false alarm rate and 100%. Reaction times were measured with millisecond resolution, and the measure of central tendency reported is the median (because reaction time distributions can be skewed due to the physiological limit on lever release times). As the reaction time procedure produces response latencies that lengthen with decreasing stimulus intensity, indicative of decreased discriminability at lower intensity levels, drug effects at different performance levels were examined by comparing reaction times for different stimulus intensities. For the auditory stimuli, intensities at high, medium, low, and below-threshold levels were used that were approximately 25, 15, 5, and −5 dB, respectively, relative to an animal's auditory threshold; for the visual stimuli, the intensities at high, medium, low, and below-threshold levels were comparably selected at 12.5, 7.5, 2.5, and −2.5 dB, respectively, relative to an animal's visual threshold.

Performances for nondrug sessions were considered stable when: a) A session contained three or more successive threshold estimates that varied by no more than ±1.25 dB for visual thresholds and by no more than ±2 dB for auditory thresholds; b) false alarm rates were below 30% for each block of trials within a session; c) all successive median reaction times for the highest stimulus intensity were within 50 ms of one another for all test blocks of a session; and d) no systematic changes occurred in either thresholds or reaction times across blocks of trials within a session. Differences in the above criteria for auditory and visual thresholds relate to the behavioral variability in sensory thresholds and the differing physical measurement units employed for auditory and visual stimuli.

Data Analysis

Both increases and decreases in the sensory threshold and reaction time measures were examined as a function of drug dose. For elevations in these performance measures, the block of trials for which the greatest increase occurred was taken as the maximum or "peak" effect of the drug dose given prior to the session. Similarly, the block of trials for which the greatest decrease occurred was taken as the minimum effect of the drug dose given. Changes in these maximum and minimum performance measures were compared to similarly derived maximum and minimum changes for saline control sessions, resulting in performance change measures for thresholds and reaction times that could then be compared across subjects and modalities.

Drug Administration

Once training was complete, the effects of acute injections of cocaine were examined by injecting animals with cocaine HCl once or twice weekly (typically on Tuesdays and Fridays). Cocaine HCl was diluted in 0.9% NaCl with the total concentration adjusted to yield the appropriate dose at 0.5 ml volume. During sessions when cocaine was not administered, 0.5 ml NaCl was injected. Cocaine and saline were administered via IM injections into the gluteal region of the baboons. Each single injection occurred immediately prior to the session in the test chamber and was given at approximately the same time every day. The actual injection site was varied from day to day to avoid tissue damage from frequent injections. The doses examined were 0.001, 0.0032, 0.01, 0.032, 0.1, 0.32, 0.56, 1.0, and 1.8 mg/kg. Doses were given in an ascending/descending order. Each dose was administered at least twice. The higher doses of cocaine typically produced long pauses before a baboon would initiate responding, occasionally resulting in fewer trials per session and longer sessions. During these cocaine-induced initial pauses, several pellets were manually delivered at about 20-min intervals until baboons began lever pressing. For each baboon, there was a dose at which no responding occurred within 2 h.

RESULTS

Figure 1 shows reaction times as a function of stimulus intensity for both the auditory and visual reaction time procedures (top and bottom graphs, respectively) following IM administration of either saline (○) or cocaine (●). Each point is the mean of the four to five median reaction time estimates obtained during each session. Reaction times are shown for 0.32 mg/kg cocaine for the auditory reaction time procedure and 0.032 mg/kg cocaine for the visual reaction time procedure. Based upon dose–effect functions (shown in Fig. 4), these cocaine doses were the most effective in consistently affecting reaction times. Error bars encompass the interquartile range, or middle 50% of each distribution, about each saline data point. All reaction time functions showed the normal decrease in reaction time as well as in the variability in reaction times as stimulus intensity increased. As is typical, control visual reaction times were slightly longer than control auditory reaction times. Following cocaine, animals showed decreases, or shortenings, in reaction times for both auditory and visual stimuli. These lowered reaction times fell outside of the interquartile range in only three instances but were consistent both within and across animals at all but the lowest stimulus intensity.

Figure 2 shows frequency distributions of the reaction times displayed in Fig. 1 for two baboons showing the most consistent reaction time changes. Shown from left to right are distributions for the high, medium, and low stimulus intensities, respectively (25, 15, and 5 dB, relative to auditory threshold; 12.5, 7.5, and 2.5 dB, relative to visual threshold). The first two rows of graphs show distributions of baboon BE's auditory reaction times following saline and 0.32 mg/kg cocaine, respectively; the last two rows of graphs show distributions of baboon ER's visual reaction times following saline and 0.032 mg/kg cocaine, respectively. For both animals, reaction time distributions at the two higher stimulus intensities were shifted toward lower values and were also less variable following cocaine. Baboon ER's reaction times for the intensity just above threshold were similarly affected. No such trends were evident at intensities just above threshold for baboon BE. At intensities below threshold levels (not shown), reaction times were randomly distributed for both animals. Reaction time distributions from other baboons showed similar changes at these doses. Relative changes in the medians of these reaction time distributions were compared across the

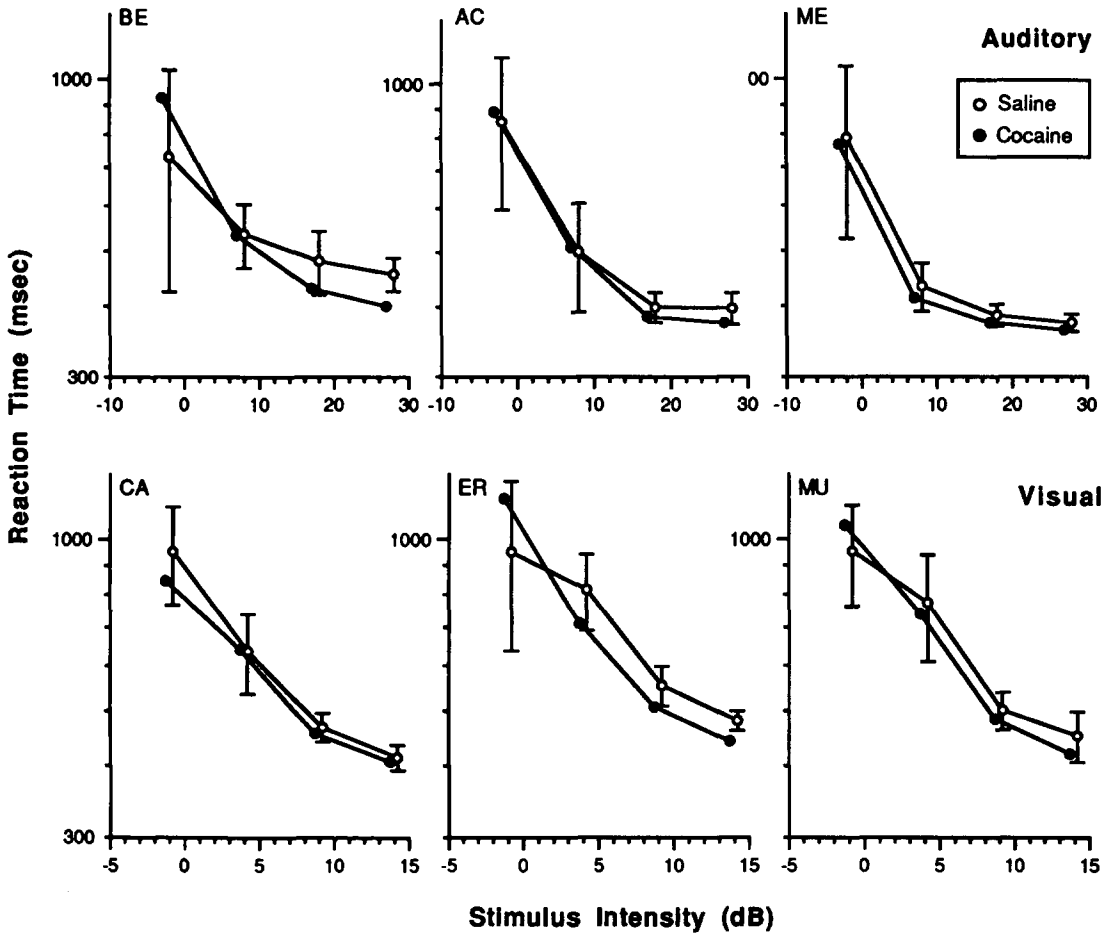

FIG. 1. Mean reaction times as a function of stimulus intensity for both the auditory and visual reaction time procedures (top and bottom graphs, respectively) following IM administration of either saline (○) or cocaine (○). Mean reaction times are shown for the most effective cocaine dose (0.32 mg/kg for the auditory reaction time procedure and 0.032 mg/kg for the visual reaction time procedure). Error bars encompass the interquartile range for each saline data point. Saline and drug functions are slightly offset for clarity.

different stimulus intensities as well. Plots of the percentage decrease in median reaction times from vehicle reaction time values (not shown) indicated that neither the shorter nor longer reaction times associated with the various stimulus intensities were differentially affected within a session (i.e., the degree of change did not depend upon the baseline reaction time value).

Figure 3 shows the time course of cocaine's effects in plots of median reaction times as a function of session time for the auditory reaction times of baboon BE (left) and the visual reaction times of baboon ER (right) following cocaine doses of 0.32 and 0.032 mg/kg, respectively. The top, middle, and bottom graphs in each column of Fig. 3 show reaction times for high, medium, and low stimulus intensities, respectively. For each graph, median reaction times were computed for 25-trial blocks (5 trials per stimulus intensity) across the entire session to produce a time course of changes in reaction times (not enough reaction times occurred at the below-threshold intensities to generate meaningful time course plots at these intensities). All warm-up trials were included to observe any possible time course effects early in the session. Baboon BE (left) did not respond until 40 min postinjection following 0.32 mg/kg cocaine. Once responding began, however, median reaction times at the highest intensity decreased and remained below the previous day's control reaction time levels for the remainder of the session. At the middle intensity, reaction times were also generally below saline control levels for the remainder of the session; at the lower intensity, reaction times during both saline and cocaine sessions were more variable, with no consistent differences evident. At the 0.032-mg/kg dose of cocaine, baboon ER did not pause as long as baboon BE but did show similar changes in visual reaction times. For baboon ER, the data following both saline and cocaine showed a pronounced warm-up effect during the second 20 min of the session, with reaction times for both the high and middle intensities decreasing gradually over this period. Between 40 and 50 min postdrug, however, reaction times to the high and middle intensities decreased more so following cocaine than following saline. As with baboon BE, baboon ER showed considerably more variability in reaction times at the low intensity. The time course of changes in reaction times for other baboons were similar to those of baboon BE.

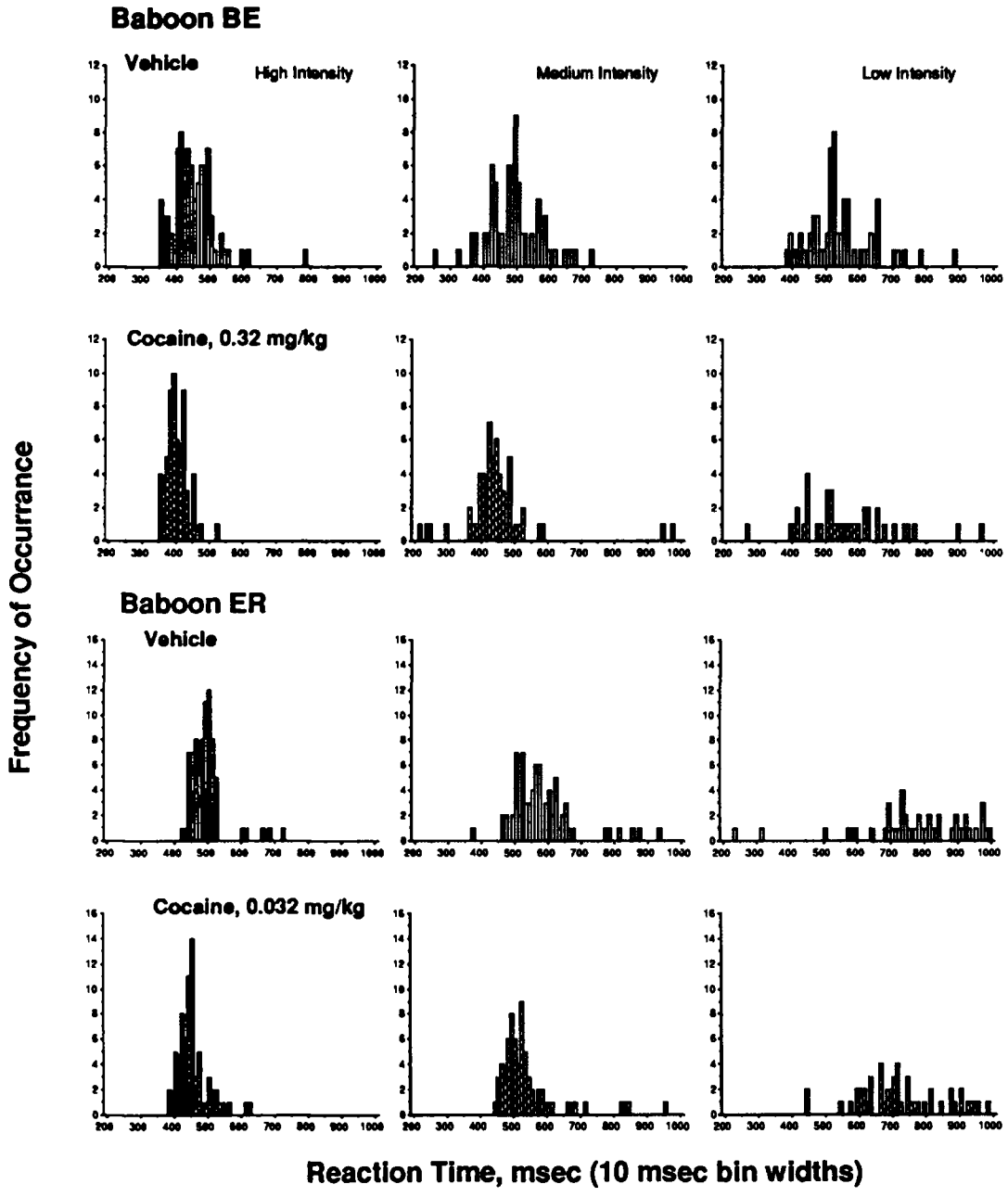

FIG. 2. Frequency distributions of the reaction times displayed in Fig. 1. Distributions of reaction times for the high- to low-intensity stimuli are shown from left to right. Top two rows, distributions of baboon BE's auditory reaction times following saline and 0.32 mg/kg cocaine, respectively; bottom two rows, distributions of baboon ER's visual reaction times following saline and 0.032 mg/kg cocaine, respectively.

The data of Fig. 3 indicate that cocaine's effects on reaction time can follow a time course of change across a session, with the most pronounced effects occurring later within the 2-h experimental sessions. Thus, the data shown in Figs. 1 and 2 may represent an average of cocaine's effects over a time period when the drug's effects are varying. To determine the maximum, or "peak," effect of cocaine in reducing reaction times, the minimum values for both reaction times and sensory thresholds were determined for each session for all baboons. Figure 4 shows these minimum values in sensory thresholds (top) and reaction time performances for the highest stimulus intensity (bottom) as a function of cocaine dose for all baboons. Auditory and visual sensory motor functions are shown to the left and right, respectively. Each function represents the differences between the mean threshold and reaction time measures during the immediately preceding nondrug day and the minimum thresholds and reaction times observed during the four to five blocks of trials for the following day's drug session, averaged across replications at each drug dose for each animal. Control data points represent similarly

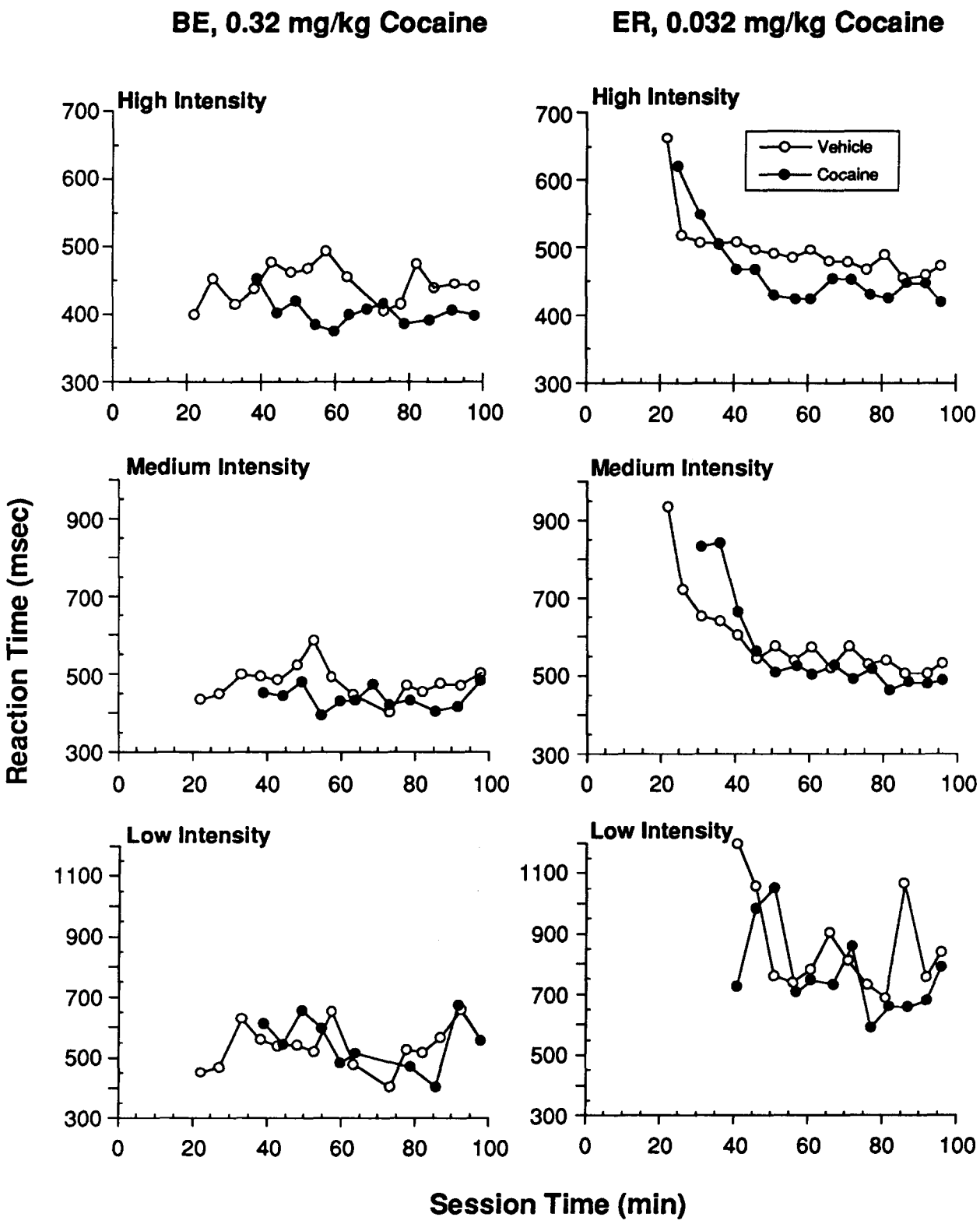

FIG. 3. Median reaction times as a function of session time for the auditory reaction times of baboon BE (left) and the visual reaction times of baboon ER (right) following cocaine doses of 0.32 and 0.032 mg/kg, respectively. The top, middle, and bottom graphs in each column show reaction times for high, medium, and low stimulus intensities, respectively. Each median reaction time point is based upon 25-trial blocks (5 trials per stimulus intensity).

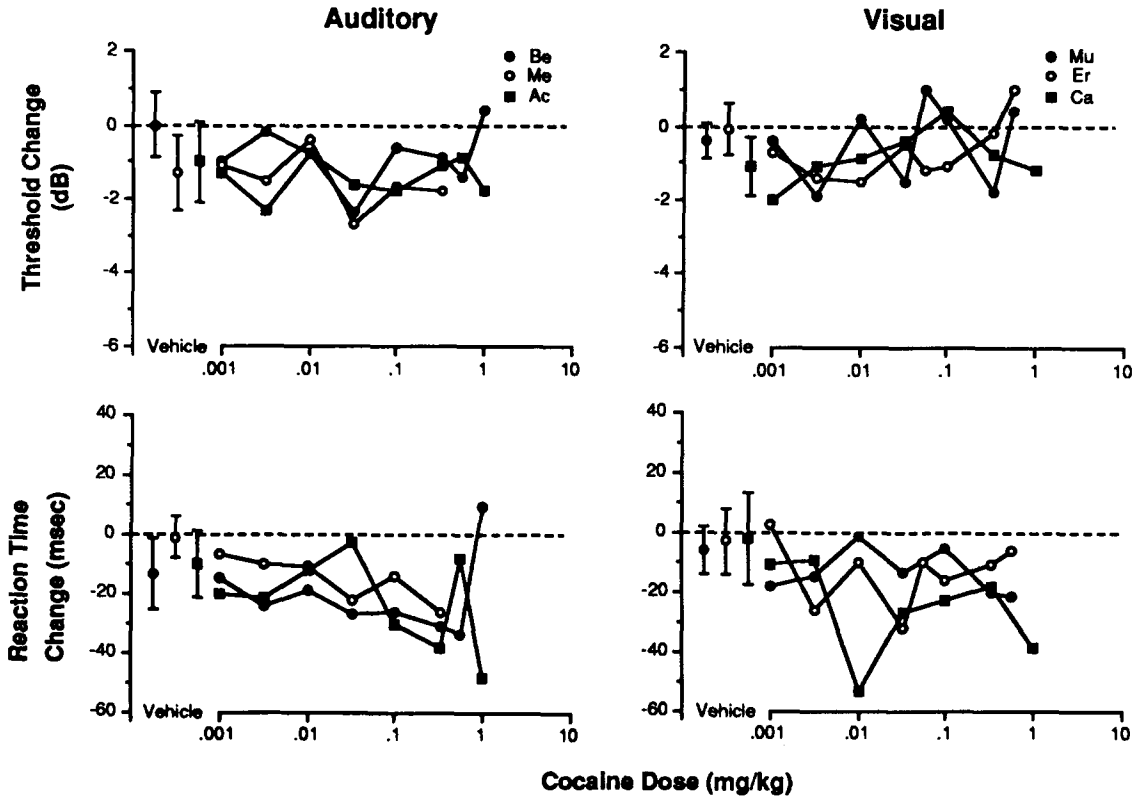

FIG. 4. Minimum changes in sensory thresholds (top) and reaction time performances (bottom) as a function of cocaine dose for all baboons. Auditory and visual sensory motor functions are shown to the left and right, respectively. Each function represents the differences between the mean threshold and reaction time measures during the immediately preceding nondrug day and the minimum threshold and reaction time observed during the drug session, averaged across replications at each drug dose for each animal. Control data points represent similarly derived measures following consecutive saline sessions, with error bars encompassing 95% confidence limits. Baseline reaction times were as follows: 371 ms (AC), 449 ms (BE), 359 ms (ME), 450 ms (CA), 469 ms (ER), and 402 ms (MU).

derived measures following consecutive vehicle sessions, and error bars encompass the 95% confidence limits. The data of Fig. 4 show prominent decreases in auditory and visual reaction times following cocaine. The auditory reaction time functions decreased across the dose range studied, with the most consistent effect occurring at 0.32 mg/kg cocaine. At this latter dose, reaction time decreases averaged 7.0, 10.1, and 7.2% below baseline levels for baboons BE, AC, and ME, respectively. Baboon ME did not respond at higher doses and baboons BE and AC performed somewhat erratically at these higher doses, often pausing for over 1 h before beginning to respond in the procedure. While the visual reaction time functions were also below the zero change point, they were more variable and did not show greater decrements as a function of dose for any subject. On average, the largest decrements in visual reaction times occurred at the 0.032-mg/kg cocaine dose, which produced average reaction time decreases of 6.9, 3.1, and 6.1% for baboons ER, MU, and CA, respectively. Animals differed in their sensitivity to cocaine doses. Baboon ME was the most sensitive and did not respond in the procedure at doses above 0.32 mg/kg; all baboons ceased responding at 1.8 mg/kg cocaine. No systematic differences in these effects of cocaine on reaction times were found as a function of animals' prior drug histories.

Figure 5 summarizes the sensory motor effects of cocaine by showing changes in sensory thresholds (top) and reaction time performances for the highest stimulus intensity (bottom) as a function of cocaine dose, averaged across all animals. Each graph shows the average minimums (bottom function, ■) and the average maximums, or "peak effects" (top function, ●), observed for each performance measure. Single points represent similarly derived vehicle control performances with error bars encompassing 95% confidence limits. For both auditory and visual thresholds (upper graphs), these minimum and maximum functions are displaced approximately equally above and below the zero change point (broken line), indicating that over this cocaine dose range neither auditory nor visual threshold sensitivities were consistently elevated or lowered following cocaine. On the other hand, both auditory and visual reaction times were systematically affected, with increasing cocaine doses producing shortened minimum reaction times in particular. The maximum reaction time functions also showed reductions below the zero change point, which again indicates a general effect of cocaine to reduce reaction times of differing lengths.

Observations of subjects via infrared cameras indicated that following administration of low doses of cocaine little change was seen in typical cage behaviors. Following high

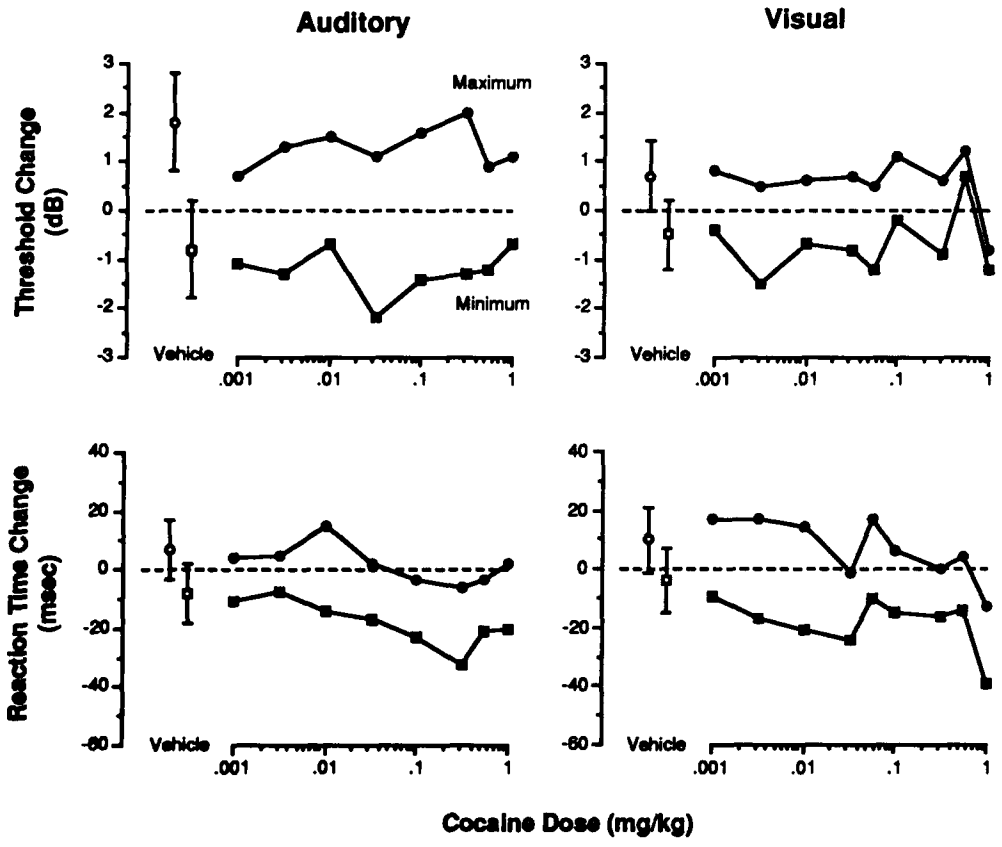

FIG. 5. Changes in sensory thresholds (top) and reaction time performances (bottom) as a function of cocaine dose, averaged across all animals. Each graph shows the average maximum (top function, ●) and average minimum (bottom function, ■) changes observed for each performance measure. Single points represent similarly derived vehicle control performances with error bars encompassing 95% confidence limits. At cocaine doses of 0.56 and 1.0 mg/kg, data points were based upon averages with $n < 3$.

cocaine doses, however, some subjects developed repetitive, stereotypic motor patterns. Baboon AC, for example, engaged in right-angle head turns approximately 5–10 min following these higher doses, which persisted for approximately the duration of the cocaine-induced pausing during the first part of the behavioral sessions. Complete inactivity was observed for baboon MU, on the other hand, during these cocaine-induced pauses. All other subjects showed no specific gross motor behavior changes, although lengthy pausing was still obtained with each subject at the higher cocaine doses. Pellets were occasionally delivered independent of behavior during these periods but did not elicit responding and were generally not eaten during these pauses. The responding of all subjects was easily disrupted by loud external noises penetrating the sound-attenuating chambers during these sessions, whereas such noises did not disrupt responding during control sessions. Baboons showed no aberrant behaviors on return to their home cages except for an occasional lack of the acceptance of food. On days following acute cocaine administration, there were no observable abnormal behaviors and no baboon showed continued maintenance of shortened reaction times on these days.

DISCUSSION

The present results demonstrate that acute administration of cocaine can selectively reduce auditory and visual reaction times while having little effect on auditory and visual threshold sensitivities. These shortened reaction times occurred not only in response to a high-intensity, clearly detectable stimulus but also to lower-intensity stimuli that were just above threshold levels and presumably more difficult to detect. The reductions in reaction times were more consistent and reliable at the higher-intensity stimuli, as evidenced in the tighter, more narrow reaction time distributions at these intensities compared to the lower intensities. Although reaction time distributions for the differing intensity levels showed a considerable shift to shorter reaction times with cocaine administration, compared to previous saline sessions there was less overlap for the high-intensity latency distributions than for the low-intensity latency distributions. Further, the distributions shown may underestimate cocaine's full effects because these distributions were for reaction times throughout an entire session (i.e., data were included that were likely obtained prior to full onset of the drug's effects). Thus, cocaine's effects on reaction time were more easily observed as well as more

consistent for reaction times to stimuli well above threshold levels.

There are a number of possibilities for the described effects of cocaine on reaction times. First, shortened reaction times would be expected if cocaine lowered the threshold for the sensory stimuli employed. Lowered auditory thresholds might result in an increase in the perceived "loudness" of the auditory stimuli employed because reaction times normally vary inversely with stimulus intensity (25) and are indicative of changes in loudness of acoustic stimuli in both humans and monkeys (20,21). In the present study, however, no indications were found of cocaine lowering auditory or visual thresholds, suggesting that threshold sensitivity changes were not an underlying factor in the observed reaction time effects.

A second possibility is that cocaine increased stimulus "reactivity" in some manner in the absence of any sensory changes at or near threshold. Cocaine's effects on the acoustic startle response, for example, indicate a dose-related increase in the amplitude of the startle response in rats, an effect ascribed to cocaine's ability to increase dopamine transmission by blocking dopamine reuptake (2). As cocaine does not augment electrically elicited startle, it appears that cocaine acts by modulating neural activity relatively early in the startle reflex pathway and thus primarily affects the auditory sensory system rather than any motor output system in the reflex (7). While the present results suggest that cocaine does not affect behaviorally determined auditory threshold sensitivity, the possibility remains that cocaine may affect other aspects of hearing such as suprathreshold loudness functions. Abnormal increases in loudness (auditory "recruitment") are common in humans with a monaural hearing loss. A loss in sensitivity occurs in one ear, for example, while intense stimuli are perceived as equally loud in both ears, resulting from an increased growth in loudness in the damaged ear to "catch up" to the perceived loudness in the normal ear. Such loudness effects have been demonstrated experimentally in monkeys (20,21) and result in reaction times that shorten more rapidly as a function of stimulus intensity over a limited range of stimulus intensities (20). As these effects have thus far been demonstrated only following experimentally induced hearing losses, it is unclear whether such changes in the perceived stimulus magnitude may be occurring following cocaine. Further, it is not known whether similar effects may occur in the visual system.

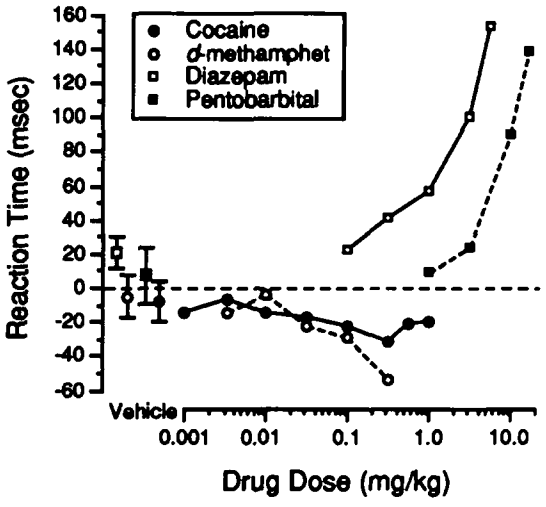

FIG. 6. Changes in auditory reaction time performances as a function of drug dose for cocaine, *d*-methamphetamine, diazepam, and pentobarbital. For cocaine and *d*-methamphetamine, each function represents the average minimum changes; for diazepam and pentobarbital, each function represents the average maximum changes. Single points represent similarly derived vehicle control performances with error bars encompassing 95% confidence limits.

A more parsimonious explanation, on the other hand, is that the observed reductions in reaction times following cocaine are a motor response effect because cocaine is known to produce increases in motor activity similar to those of other psychomotor stimulants [cf. (14)]. This view is consistent with the observed reaction time changes being similar for both auditory and visual stimuli. Further, as the reaction time and threshold measures obtained with the reaction time procedure do not necessarily covary (10,11) any motor changes need not be accompanied by cocaine-related sensory changes for auditory and visual modalities as well. While this hypothesis is not consistent with the lack of cocaine's effects on electrically elicited acoustic startle mentioned above (7), major differences may exist between the acoustic startle response and the well-practiced performances examined with the reaction time procedure. Further, recent studies in humans do indicate increases in both subjective (5) and objective (12) performance measures following cocaine.

Enhancement of performance has been suggested as one effect that maintains continued cocaine use. The present data suggest that cocaine may, under certain circumstances, shorten the latency of responding to visual and auditory stimuli and may, in addition, reduce the variability in these reaction time performances. These results parallel the reaction time decreases seen with *d*-methamphetamine administration in baboons (11) and are in contrast to the reaction time-elevating effects of such compounds as pentobarbital (10), diazepam (19), ethanol (8,9), and opiates (24). Figure 6 shows a comparison of the dose-related effects of cocaine with similarly derived changes produced by *d*-methamphetamine, diazepam, and pentobarbital [data taken from (11,19,10), respectively] for auditory reaction times. While diazepam and pentobarbital produce dose-dependent increases in auditory reaction times, both cocaine and *d*-amphetamine produce dose-related decreases. The magnitude of these reaction time decreases may be subject to a floor effect due to the physiological bounds on minimum reaction times. The present performance changes were derived under sound- and light-attenuated conditions with highly practiced performance; nevertheless, others have already pointed to the often perceived importance of the "edge" that other stimulants may provide in highly practiced athletic performances (17) as well as in other complex performances. The extent to which similar changes in performance might be observed under other conditions with cocaine remains to be determined. Under the present conditions, however, cocaine also suppressed responding during the first hour following administration. Further, it is not known whether or how different schedules of drug administration or longer-term cocaine administration may affect such performances.

ACKNOWLEDGEMENTS

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