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Perceptual and motor effects of morphine and buprenorphine in baboons

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Abstract

The effects of morphine and buprenorphine on auditory perceptual discriminations and response latency (''reaction time'') in baboons are compared. The task employed synthetic human vowel sounds that are readily generated in the laboratory, and closely approximate natural baboon ''grunt'' vocalizations [J. Acoust. Soc. Am. 101 (1997) 2951]. Baboons pressed a lever to produce one repeating ''standard'' vowel, and released the lever only when one of four other ''comparison'' vowels occasionally occurred in place of the standard vowel. The percentage of correct detections and median reaction time for each comparison were measured following intramuscular drug administrations of morphine (0.01–1.8 mg/kg) and buprenorphine (0.00032–0.032 mg/kg). Both morphine and buprenorphine impaired vowel discriminability, and greater impairments occurred for those comparison vowels that were more similar in formant structure to the standard vowel. Morphine increased reaction time in all baboons, and buprenorphine increased reaction time in two of three baboons. Morphine's perceptual effects occurred within 20–40 min following drug administration; buprenorphine's perceptual effects occurred 50–100 min following drug administration. Morphine and buprenorphine did not differ in the time course of their maximal reaction time effects. The results demonstrate that both morphine and buprenorphine can impair auditory discriminations involving human vowel sounds in baboons, as well as lengthen reaction times to the stimuli.

Keywords: Morphine; Buprenorphine; Auditory perception; Discrimination; Motor function; Baboon; Lever release

1. Introduction

Opioids have been shown to affect not only the perception of pain, but also perception in other modalities such as audition and vision. For example, morphine impairs the accuracy of rats in making both click and tone discriminations in the presence of background masking noise (Hernandez and Appel, 1979; Koek and Slangen, 1983), in discriminating the position of a light flash (Grilly et al., 1980), and in acquiring conditioned responses to both tones and lights (Schindler et al., 1984, 1985). In pigeons, morphine impairs visual color discrimination accuracy (West et al., 1982; Nielsen and Appel, 1983), and increases the percentage of errors in a repeated acquisition procedure (Thompson and Moerschbaecher, 1981). In general, these perceptual effects of morphine have been attributed to an effect on sensory or discrimination processes rather than changes in the organism's responsivity in the discrimination procedure (for review see Appel and Dykstra, 1977; Heise and Milar, 1984). Morphine-induced changes in perceptual function have not, however, been as readily demonstrated with nonhuman primates (for example, see Milar and Dykstra, 1985; Moerschbaecher et al., 1984; Moerschbaecher and Thompson, 1983; Samra et al., 1985), suggesting the possibility of a substantial species difference in morphine's effects on perceptual processes.

Research from this laboratory with baboons has also failed to demonstrate that either morphine or another common drug of abuse — cocaine — affects the detectability of simple tones or white light (Spear et al., 1992; Hienz et al., 1993, 1994). On the other hand, it has recently been shown that cocaine does impair the ability of baboons to perform another type of auditory discrimination — the discrimination of human speech sounds (Hienz et al., 1995, 1996). This

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result suggests the possibility that speech sound discriminations may be more susceptible to the effects of drugs than discriminations involving simple tones or white light, and that the use of speech sound discriminations may provide a better test of the possible perceptual effects of morphine.

There is evidence indicating that the discrimination of human speech sounds by nonhuman primates is a perceptual task more akin to those types of auditory discriminations made in the natural environment. First, there is a close resemblance between many human speech sounds and nonhuman primate vocalizations (Snowdon et al., 1982). Second, the acoustic properties of baboon *grunt* calls are extremely vowel-like, so much so that *grunt* calls have been referred to as "prototypical human vowel sounds" (Owren et al., 1997). Third, this acoustic similarity of baboon *grunt* calls to human vowels is paralleled by a functional similarity in the use of these types of signals in that (1) baboon grunts primarily cue individual identity; and (2) human vowel sounds also play a predominant role in cueing individual identity, while conveying relatively little linguistic information (Owren et al., 1997). Thus discriminations involving vowel sounds may not only be more sensitive indicators of drug effects as noted above, but also be more representative of discriminations of biological relevance for baboons.

The present experiment examined the effects of both morphine and buprenorphine upon speech sound discriminations in baboons. Buprenorphine was examined in the present study because previous research in this laboratory indicated differential sensory effects for buprenorphine and morphine in that buprenorphine raised thresholds for the detection of both auditory and visual stimuli in baboons, whereas morphine did not (Spear et al., 1992). Buprenorphine is a mixed agonist/antagonist that produces positive subjective reactions similar to that of morphine (Lukas et al., 1983), and has been a compound of great interest due to its ability to attenuate the subjective "high" effects of morphine (Bickel et al., 1987). Further, there has been interest in buprenorphine as a pharmacotherapy for abuse of both cocaine and heroin, since buprenorphine reduces self-administration of these drugs (e.g., Carroll and Lac, 1992; Carroll et al., 1992; Mello et al., 1989, 1990).

2. Method

2.1. Subjects

Five adult male baboons (*Papio anubis*) weighing between 25 and 33 kg served as subjects. 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.). Animal care was in accordance with current NIH guidelines concerning the humane treatment of nonhuman primates.

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 that served 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.

The speech sound stimuli employed consisted of synthetic vowel sounds that were presented through a wide-range speaker located outside and above the test cage, approximately 20 cm above the ear level of a baboon's head as he sat inside the test cage. The vowels employed were /⊃/, ("aw" as in caught), /ɛ/ ("eh" as in let), /a/ ("ah" as in lot), /æ/ ("ae" as in cat), and /U/ ("uh" as in book). All vowels were generated by an Echo II speech synthesizer. Each vowel sound consisted of a repeating periodic acoustic wave form with a fundamental pitch frequency of 122 Hz; each vowel was 120 ms in duration, was presented at a rate of 2/s, and at an average intensity of 73 dB sound pressure level (SPL). All vowel stimuli were passed through a Coulbourn Instruments attenuator and a Crown D-60 amplifier, and then to the speaker. The vowels differed from one another in the location of their major frequency bands of energy, or "formant peaks." Table 1 presents the values of the formant peaks of the first and second formants of each vowel (F_1 and F_2) in Hertz, as determined via a standard linear predictive coding model. Compared to the vowel "aw," for example, the vowel "uh" has roughly equivalent changes in F_1 and F_2 while the vowel "eh" has a relatively large difference in F_2 but only a small difference in F_1.

Table 1
First and second formant frequencies (F_1, F_2) and differences (ΔF_1, ΔF_2) from the standard vowel "aw" for all vowels

Vowel symbol	Phonetic sound	F_1 (Hz)	ΔF_1 (Hz)	F_2 (Hz)	ΔF_2 (Hz)
/⊃/	"aw"	593	–	1039	–
/æ/	"ae"	726	133	1724	685
/e/	"eh"	636	43	1674	635
/U/	"uh"	463	– 130	1319	280
/a/	"ah"	649	56	1237	198

2.3. 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 vowel sound (e.g., "aw" - "aw" - "aw" - "aw" - "aw", etc.), and to release the lever only when a different, or "comparison" vowel began alternating with the standard vowel (e.g., "aw" - "aw" - "aw" - "*ah*" - "aw" - "*ah*," 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 vowel pulses (2/s) began. One of the four comparison vowels was randomly selected to alternate with the standard vowel on each trial. This change in vowel sounds between the standard vowel and the chosen comparison vowel began at a random time of between 1 and 7 s following the initial lever press. Two presentations of the comparison vowel alternated with the standard vowel (e.g., "aw" - "aw" - "aw" - "*ah*" - "aw" - "*ah*"). This resulted in a vowel alternation interval 1.5 s in duration, as measured from the onset of the first comparison vowel. Release of the lever at any time within this 1.5-s interval was reinforced with one banana-flavored pellet, following which all vowel sounds and the cue light 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 vowel changes produced an 11- to 15-s timeout from the contingencies, signaled by terminating the cue light. Failure to detect the vowel change, as indicated by holding the lever through the 1.5 s of the vowel alternation period, resulted in the termination of the cue light and the vowel sounds; 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 vowel alternated with itself throughout the trial. Lever releases during catch trials also produced a timeout of 11 to 15 s. The vowel "aw" was employed as the standard vowel and the remaining four vowels served as comparison vowels.

2.4. 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 this time baboons typically performed five full blocks of trials, i.e., 500 discrimination trials. For each comparison vowel, 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 vowel 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 vowel were timed from the onset of the first presentation of a comparison vowel to the release of the lever. Median reaction times for correct releases to each comparison vowel 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 vowels 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 both morphine and buprenorphine lengthened reaction times, the "maximal effect" of the drugs on reaction-time values was calculated by selecting the longest median reaction time from among the four to five blocks of trials of each drug session, and subtracting the median reaction time value at the corresponding time from the preceding day's saline control session. For comparison, estimates for reaction times following vehicle injections were calculated in an identical manner.

For both drugs, changes in the accuracy of the discrimination performances were assessed by examining changes in the signal-detection index d', as a function of drug dose. The d' index was calculated by transforming the percent correct scores (PC) and false alarm rates (FA) into proportions, converting them to z scores, and subtracting the FA z scores from the PC z scores ($d' = z(\mathrm{PC}) - z(\mathrm{FA})$ (Macmillan and Creelman, 1991). Because z scores for the normal distribution cannot be calculated for proportions of 0 and 1, a method suggested by Macmillan and Creelman (1991) was employed to limit proportions so that near-zero values were no lower than 1/2N, and values near 1 were no greater than $1 - (1/2N)$, where N is the number of trials employed in calculating the proportion. A "maximal effect" value in reducing discrimination accuracy was calculated for the d' index by subtracting the average d' index during the previous day's saline session from the minimum d' index during each drug session. Average values of the PC and FA scores across all four comparison vowel stimuli were employed for this analysis. Estimates of changes in the d' index following vehicle injections were calculated in an identical manner.

2.5. Drug administration

Morphine, buprenorphine, vehicle, 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. Morphine doses were adminis-

tered once or twice weekly, typically on Tuesdays and/or Fridays. To ensure adequate elimination time, buprenorphine was administered a maximum of once per week. 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 for morphine; buprenorphine was dissolved in glacial acetic acid, diluted with sterile water, and pH adjusted to 5.5 with NaOH). Because the buprenorphine vehicle was not saline, buprenorphine vehicle effects were determined for two to three additional sessions for this drug. Morphine doses administered ranged from 0.01–1.8 mg/kg; buprenorphine doses administered ranged from 0.00032–0.032 mg/kg. Doses were calculated in terms of the salts. These dose ranges 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

Fig. 1 shows the dose-related effects of morphine (top) and buprenorphine (bottom) on the discriminability of each of the four comparison vowels for each baboon. Graphs are ordered from left to right in terms of generally increasing discrimination difficulty, as judged by the performance trends observed among baboons following drug administrations. Such a trend was not observed under baseline conditions since all subjects discriminated among vowels at near-perfect levels in the absence of drug. This ordering also corresponds with a general decrease in the size of the formant differences (F_1 and/or F_2) between each comparison and the standard vowel, as shown in Table 1. Both morphine and buprenorphine reduced vowel discriminability, as indicated by decreases in percent correct scores that fell outside of the 95% confidence limits, and these reductions were more pronounced for the more difficult vowel discriminations. Following morphine (top), dose-dependent reductions in vowel discriminability were greatest for baboon WE, less so for baboon LA, and minimal for baboon DR. The significant morphine results for baboon DR were apparently a function of his consistently perfect (100%) discrimination of three of the four vowels under saline conditions. Similar reductions in vowel discriminability were observed following buprenorphine (bottom), with the decrements again being generally larger for the more difficult discriminations. Baboon KH showed large, dose-dependent decrements in discriminability with increasing buprenorphine dose, while baboon LA showed the greatest decrements at the intermediate buprenorphine dose of 0.0032 mg/kg. Baboon KE showed minimal yet statistically significant effects, apparently a function of his consistently perfect (100%) discrimination of three of the four vowels under saline conditions. None

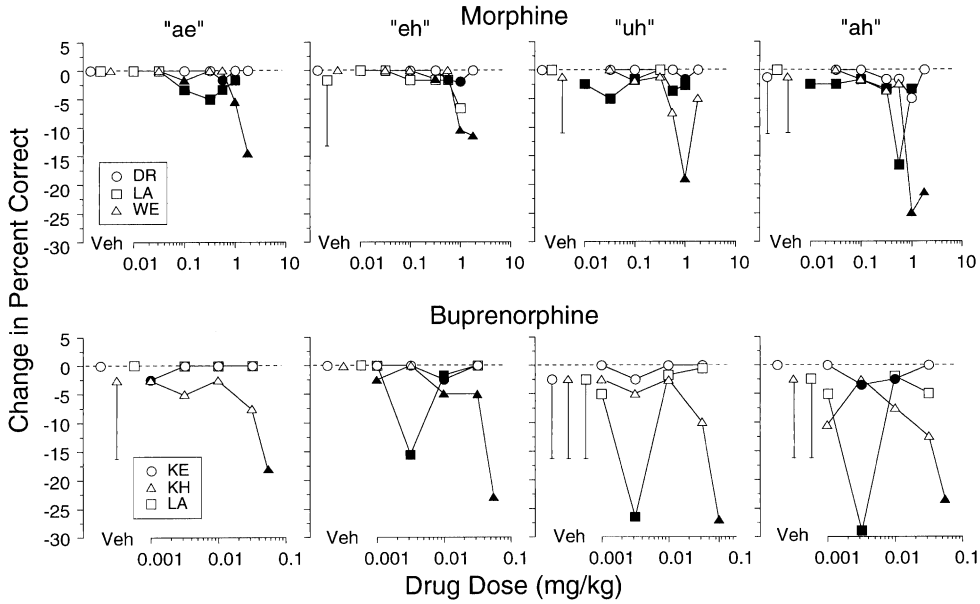

Fig. 1. The mean percentage change in the discriminability of each comparison vowel for each baboon, plotted as a function of drug dose for morphine (top graphs) and buprenorphine (bottom graphs). Each point in a graph represents the difference between the percent correct score at the time of maximal drug effect, and the percent correct score at the corresponding time from the preceding saline control day, averaged across replications at each dose. The maximal drug effect was defined as the lowest percent correct detection score obtained for a given comparison vowel among all blocks of the drug session. Saline and/or vehicle control data were derived in an identical manner. Error bars around saline and vehicle points encompass 95% confidence intervals, and are often absent due to frequent perfect (100%) scores under vehicle conditions. Filled symbols denote data points outside of the 95% confidence intervals. Graphs are ordered from left to right in terms of increasing discrimination difficulty.

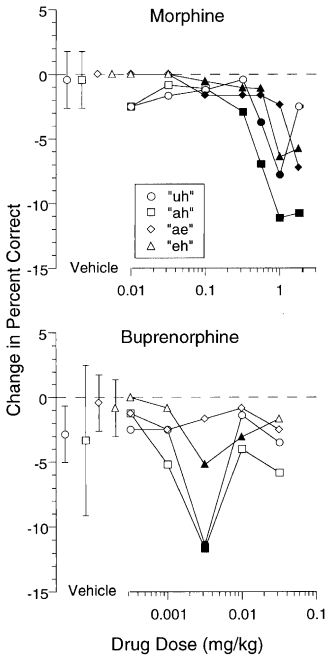

Fig. 2. Changes in vowel discriminability averaged across all animals as a function of drug dose for both morphine and buprenorphine (top and bottom graphs, respectively). Error bars encompass 95% confidence limits about the saline/vehicle points. Filled symbols denote data points outside of the 95% confidence intervals.

of the baboons showed any significant changes in false alarm rates following either morphine or buprenorphine.

Fig. 2 shows the changes in vowel discriminability averaged across all animals as a function of drug dose for both morphine and buprenorphine (top and bottom graphs, respectively). Error bars encompass 95% confidence limits about the saline/vehicle points. Discriminability generally decreased with increasing drug dose for all vowels for morphine, but not for buprenorphine due to the anomalous dip at the intermediate dose of 0.0032 mg/kg, which in turn was due in large part to baboon LA's maximal effect occurring at this dose. For both drugs, the greatest decrements occurred for the vowel "ah," the vowel most similar in formant structure to the standard vowel.

The decreases in vowel discriminability produced by morphine and buprenorphine occurred at slightly different times following drug administrations. The maximally effective doses of morphine 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 min into a session, whereupon responding was disrupted. The most effective doses of buprenorphine produced maximal changes in discriminability from 50–100 min into a session. For both drugs, baboons stopped responding about 20–30 min into a session at the highest drug doses tested. The data obtained at these high doses were included in Figs. 1 and 2 for completeness. However, these high-dose data points only indicate the effects of morphine and buprenorphine on discriminability relatively early within a session. Occasional upturns in the dose–effect functions in Fig. 1 at the high doses may thus be a reflection of this early cessation of responding during a session (e.g., Baboon WE's functions for the vowels "uh" and "ah" following morphine). Finally, the observed decreases in vowel discriminability produced by morphine and buprenorphine 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. 3 shows the dose-related effects of morphine (top) and buprenorphine (bottom) on reaction times for each baboon. The data shown are averages across all comparison vowels, since no significant differences in reaction times were observed among the different comparison vowels in the presence or absence of drug. Morphine lengthened reaction times in a dose-dependent manner for all three baboons. Again, baboon DR showed minimal effects, baboon WE showed intermediate effects, and

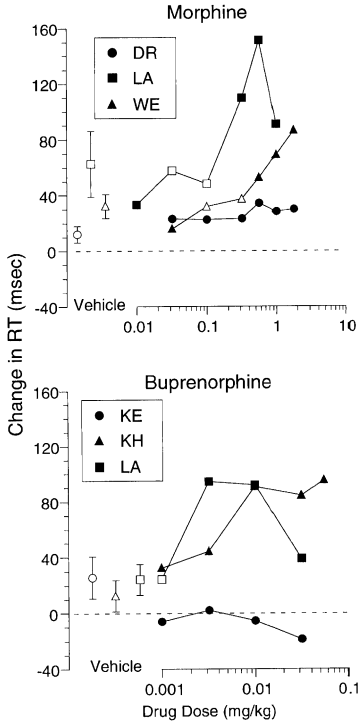

Fig. 3. Mean changes in reaction times averaged across all vowels for each baboon, plotted as a function of drug dose for morphine (top) and buprenorphine (bottom). Each point represents the difference between the median reaction time at the time of maximal drug effect, and the median reaction time at the corresponding time from the preceding saline control day, averaged across replications at each dose. The maximal drug effect was defined as the longest median reaction time found for a given comparison vowel among all blocks of a drug session. The data shown are averages across all comparison vowels, since no differences in reaction times were observed among the different comparison vowels in the presence or absence of drug. Error bars encompass 95% confidence limits about the vehicle points. Filled symbols denote data points outside of the 95% confidence intervals. Vehicle control data were derived in an identical manner.

baboon LA showed the greatest changes in reaction times. Relative to their vehicle performances, the maximum percentage increase in reaction times following morphine was 4%, 11%, and 17%, respectively, for these three baboons. Buprenorphine lengthened the reaction times of baboons KH and LA, but appeared to shorten the reaction times of baboon KE. The maximum percentage changes in reaction times following buprenorphine were 16%, 13%, and −9%, respectively, for these three baboons relative to their vehicle performances.

The differences in the magnitude of morphine's effects on reaction time appeared to be correlated with the variability in the reaction time performance in the absence of drug, since the 95% confidence limits about the morphine vehicle points were greater for those baboons showing greater increases in reaction times following morphine. The magnitude of morphine's effects on reaction times also tended to be correlated with the baseline reaction time levels of the three baboons — nondrug reaction times for baboons DR, WE, and LA being 495, 512, and 541 ms, respectively. Similar correlations of reaction time performance following buprenorphine, however, were not observed. Additionally, no obvious differences in variability or baseline reaction time levels were observed that might explain why baboon KE's reaction times were lowered following buprenorphine. For example, nondrug reaction times for baboons KH and LA during the buprenorphine testing conditions were 491 and 544 ms, respectively; and baboon KE's average reaction time of 507 ms was intermediate to these values.

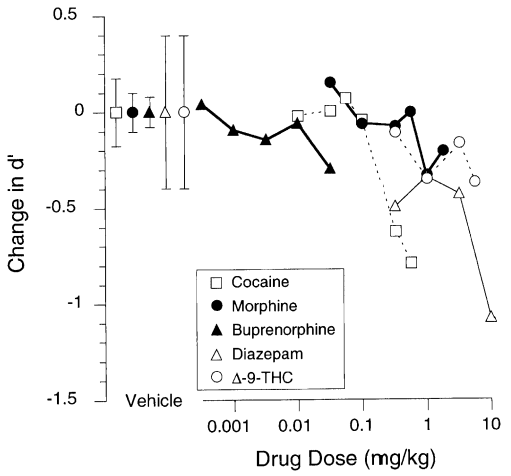

Fig. 4. The mean change in the d' index of discriminability for the comparison vowel "ah," plotted as a function of drug dose for morphine and buprenorphine in the present study, and for cocaine, diazepam, and Δ-9-THC from previously published studies (Hienz et al., 1995; Hienz and Brady, 1989). Each point represents the difference between the lowest d' index observed on drug days and the average d' index on saline/vehicle days, averaged across replications at each dose and across baboons. Saline and/or vehicle control data were derived in an identical manner. Error bars around saline and vehicle points encompass 95% confidence intervals.

The increases in reaction times produced by morphine and buprenorphine followed a similar time course of change in that both drugs produced a generally increasing 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 for both drugs. Such behavioral disruptions may be partly responsible for the occasional downturns in dose–effect functions seen in Fig. 3 (e.g., for baboon LA following both morphine and buprenorphine). The reaction time increases produced by morphine and buprenorphine 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 increases in reaction times. On the other hand, the reaction time decreases produced by buprenorphine in baboon KE were evident following the second drug dose exposures, but not during the first drug dose exposures.

Fig. 4 shows the average drug-induced changes in vowel discriminability as measured by the d' index for morphine and buprenorphine, and for cocaine, diazepam, and Δ-9-THC from previously published studies (Hienz et al., 1995; Hienz and Brady, 1989). All data are for the "ah" comparison vowel only, which tended to show the most pronounced drug effects in all studies. Both morphine and buprenorphine produced comparable decrements in vowel discriminability, with buprenorphine being much more potent in producing these changes. Both cocaine and diazepam, on the other hand, produce much greater decrements in discriminability, while Δ-9-THC has little or no effect on discriminability compared to it's range of variability under vehicle conditions.

4. Discussion

The results of the present study show clearly that both morphine and buprenorphine can impair vowel discriminability in baboons. Morphine-induced perceptual changes had been previously demonstrated in rats and pigeons but not in nonhuman primates, suggesting a possible species difference in morphine's effects on perceptual function. Reports of previous research in this laboratory have also described differential sensory effects for buprenorphine and morphine, with buprenorphine but not morphine raising thresholds for the detection of both auditory and visual stimuli in baboons (Spear et al., 1992). The present demonstration of clear changes in perceptual function following morphine in baboons, however, is consistent with morphine's demonstrated effects on a number of auditory discriminations in rats (Hernandez and Appel, 1979; Koek and Slangen, 1983; Grilly et al., 1980; Schindler et al., 1984, 1985). Finally, morphine and buprenorphine appeared equally effective in disrupting vowel discriminations. Given the greater intrinsic activity of morphine at μ receptors, one might have expected morphine to have had a greater effect

than buprenorphine upon these discriminations. This lack of a greater effect of morphine, however, is similar to previous research demonstrating effects of buprenorphine, but not morphine, on the detection of auditory and visual stimuli in baboons (Spear et al., 1992).

The present results also support the suggestion that speech sound discriminations of the present type are more susceptible to the effects of drugs than are discriminations involving simple tones or white light. Previous studies with baboons were unable to demonstrate effects of either morphine or cocaine on the detectability of simple tones or white light (Spear et al., 1992; Hienz et al., 1993, 1994). Both of these drugs, however, clearly impair the ability of baboons to discriminate among human speech sounds (see Fig. 4). Obviously, the acoustic structure of speech sounds is much more complex than that of simple tones, and it could be this added stimulus complexity that contributes to making the discriminations more readily subject to drug effects. On the other hand, it is not obvious why the availability of extra stimulus cues for making a discrimination might lead to more pronounced drug effects, as opposed to making the discrimination more resistant to drug effects. Additionally, there is no one-to-one correspondence between stimulus complexity and ease of discrimination for acoustic discriminations; noise bursts, for example, have an exceedingly complex acoustic structure but are not as readily discriminated as speech sounds and animal communication sounds (Sommers et al., 1992). More likely, ''ease of discrimination'' relies on the degree to which the acoustic features of stimuli match the CNS encoding abilities of the discriminating organism. The communication sounds of many nonhuman primates and birds, for example, possess precisely those characteristics to which the auditory CNS is highly tuned to receive, and has led to the suggestion of a coevolution of the mechanisms of sound production and sound perception in many species (Dooling, 1980; Brown et al., 1994).

As noted in the Introduction, the close acoustic and functional similarities between baboon grunts and human vowels make the discrimination of vowel sounds a more ''natural'' one in that it is more akin to the types of auditory stimulus discriminations made in the natural environment. Indeed, similarities between human speech and animal vocalizations have also been demonstrated in terms of how they are perceived by both humans and other animals, and how they are processed by the auditory system (Stebbins and Berkley, 1990; Frisina et al., 1996; Brown and May, 1990). One could as well argue, however, that a more ''natural'' discrimination would also be more easily learned and less readily susceptible to pharmacological disruption. Previous data on the acquisition of these discriminations have documented that speech sound discriminations are learned easily and rapidly, frequently requiring as few as three to five sessions before perfect discriminations are obtained, compared with the 1–2 month periods required for stable performances on detection threshold tasks (Hienz and Brady, 1988). This ease of learning is likely due to the wide variations in frequency, intensity, harmonic content, and acoustic ''transients'' (e.g., sharp changes in the amplitude and/or frequency of acoustic signals) contained in both human and animal vocalizations. Given such a rich variety of stimulus changes upon which this type of perceptual discrimination can be based, it might thus appear surprising to observe pharmacological disruptions of these discriminations.

Drugs such as diazepam, cocaine, and Δ-9-THC, however, do impair the perception of vowel sounds (Hienz et al., 1993, 1995; Hienz and Brady, 1989); in addition, both diazepam and cocaine have been shown to have little effect on auditory detection thresholds for simple tones (Hienz et al., 1994; Lukas et al., 1985). In these previous studies, the effects of these drugs on speech sound discriminations could not be attributed to a general decrement in overall performance, since the drugs differentially affected other aspects of the discriminations. For example, diazepam lengthened reaction times to the vowel stimuli (Hienz and Brady, 1988), whereas cocaine shortened reaction times (Hienz et al., 1995), and Δ-9-THC did not affect reaction times (Hienz and Brady, 1989). Since these drugs had little effect on behavioral thresholds for the detection of simple tones, their effects on speech sound discriminations suggest that the auditory perceptual effects of these drugs result from disruptions in mechanisms involved in the processing of spectral cues, or ''pitch,'' as opposed to intensity cues, or ''loudness'' (Hienz et al., 1995). Further, both diazepam and cocaine impaired vowel discriminability, more so for those vowels that are more similar to one another in formant structure — in other words, the greater the spectral differences between vowels, the smaller the drug effect (Heinz et al., 1995; Hienz and Brady, 1988, 1989) — results that also suggest drug influences on CNS mechanisms related to the processing of spectral cues. Similarly, in the present study the greatest drug-induced decrements in vowel discriminability occurred for the vowel ''ah,'' the vowel most similar in formant structure to the standard vowel. These data, coupled with the previously demonstrated lack of effects of both morphine and buprenorphine on simple tone discriminations, suggest a similar interpretation of these drugs influencing information processing of spectral frequency cues.

The lengthened reaction times following morphine and buprenorphine replicate the findings of a previous study in which these two compounds were found to lengthen reaction times to near-threshold tones and lights in baboons (Spear et al., 1992). In that study the effective doses for significantly elevating auditory reaction times were 0.56 mg/kg for morphine and 0.01 mg/kg for buprenorphine, doses that fall within the effective dose ranges for the reaction-time data of Fig. 3. Additionally, the effects of both morphine and buprenorphine in this latter study were considered not to be a generalized effect on either overall performance or stimulus control since (1)

morphine did not produce any sensory effects and (2) buprenorphine differentially affected the detection of low-intensity and high-intensity stimuli within the study. Similarly, the present effects of morphine and buprenorphine on the perceptual and motor aspects of the behavioral performances do not appear to be a generalized effect upon behavior since the observed motor effects were comparable across all vowels, whereas vowel discriminability was differentially affected as a function of the similarities in formant structure between standard and comparison vowels. The results thus demonstrate that both morphine and buprenorphine can selectively impair auditory discriminations involving human vowel sounds in baboons, as well as lengthen reaction times to the stimuli.

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