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Drugs and Visual Perception: Effects of LSD, Morphine and Chlorpromazine on Accuracy, Bias and Speed

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Abstract. Ten pigeons were trained to discriminate between the intensities of two white lights (projected behind a center response "key") using a discrete trial procedure in which choice behavior involved pecking at red or green lights projected behind left or right side keys. LSD (0.02–0.08 mg/kg) did not alter the accuracy of the brightness discrimination (percent correct) although it did lower response speed and may have differentially affected spatial (position) bias. Morphine (2.5–10.0 mg/kg) decreased accuracy of discrimination as well as response speed and had greater effects on trials when the bright stimulus was presented than when the dim stimulus was presented. Chlorpromazine (7.5–30.0 mg/kg) lowered accuracy without significantly altering any other measure of performance.

Key words: (Visual) Discrimination – Perception – Bias – Lysergic acid diethylamide (LSD) – Morphine – Chlorpromazine – Pigeons

While psychoactive drugs with diverse pharmacological properties (e.g., hallucinogens, opiates, neuroleptics) alter discrimination performance, analysis of the nature of these alterations and the mechanisms that underlie them has proven to be difficult. This is at least in part because perceptual behavior necessarily involves both stimulus (sensitivity) and response (criterion or bias) dimensions, which are often confounded (Goldiamond 1962). Moreover, recent experiments involving two-choice, discrete-trial procedures have shown that drugs may affect both of these dimensions and sometimes have inconsistent or complex effects that are difficult to interpret (Appel and Dykstra 1977). For example, the hallucinogen lysergic acid diethylamide (LSD) is believed to distort various sensory processes (Sankar 1975), but systematic changes in accuracy of auditory (Dykstra and Appel 1970, 1972, 1974; Hernandez and Appel 1979), visual (Appel and Dykstra 1977; Straub and Appel 1975), footshock (Hernandez and Appel 1979), or temporal (Altman et al. 1979; Dykstra and Appel 1974) discrimination following this compound at doses sufficient to lower response speeds do not in fact occur, at least in rats and pigeons. However, LSD sometimes alters response bias in auditory frequency (Dykstra and Appel 1974), auditory or visual duration (Altman et al. 1979; Dykstra and Appel 1974), and visual intensity (Straub and Appel 1975) discrimination tasks – a result that might be interpreted, erroneously, as indicating that LSD changes sensory phenomena. Unfortunately, these effects on bias do not occur consistently (Altman et al. 1979; Hernandez and Appel 1979).

The pain-reducing properties of morphine are well-known and define one of the major clinical uses of various opiates (Jaffe 1970) but this "analgesia" is often said to involve the "reactive component of pain" rather than drug-induced decreases in sensitivity to painful stimuli (Beecher 1959). However, morphine, in contrast to LSD, decreases the ability of rats to detect or discriminate noxious stimuli such as footshock (Grilly et al. 1980; Grilly 1981; Lloyd et al. 1978; Hernandez and Appel 1979, 1980) as well as (presumably) non-noxious events such as tones in a background of "white" noise (Hernandez and Appel 1979) or the relative positions of two lights (Grilly et al. 1980). Moreover, these effects cannot be explained in terms of drug-induced changes in some non-sensory aspect of choice behavior ("the reactive component") because systematic changes in response bias do not occur following morphine (Grilly 1981; Hernandez and Appel 1980).

Neuroleptics such as chlorpromazine (CPZ) and haloperidol are believed to alter perception by decreasing responsivity to sensory stimulation (Iversen and Iversen 1975) – an "ataractic" effect that may underlie clinical efficacy (Caldwell 1978). While these compounds affect performance in rats trained to detect either shock (Lloyd et al. 1978; Hernandez and Appel 1979, 1980) or tones (Hernandez and Appel 1979), they do so, in contrast to morphine, only by increasing bias (toward false positive responses on trials when stimuli are not presented). However, in pigeons, CPZ decreases accuracy without altering bias (Altman et al. 1979; Straub and Appel 1975).

Thus, compounds from at least two pharmacological classes that are generally thought to alter perception (hallucinogens and neuroleptics) have ambiguous effects on response bias and another agent (morphine), which is thought to affect reactivity, in fact attenuates ability to discriminate (sensitivity). However, in studies of the effects of drugs on discrimination behavior discussed thus far, animals must make either a left or a right response to receive differential reinforcement in the presence of or following the stimulus to be discriminated; thus, response bias has been equated with position preference. It is entirely possible that choice behavior based on some other dimension, e.g., color, would be affected less variably by the drugs under consideration. This possibility was tested in the present experiment by using a procedure similar to that of Stubbs (1968, 1974) to analyze the effects of LSD, morphine and CPZ on a brightness discrimination. In this procedure, the subject must respond to the

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color rather than the position of two response keys to indicate its choice; this has the advantage of permitting one to observe drug-induced changes that may occur on both perceptual (brightness or color) and spatial bias (as well as upon accuracy and speed) simultaneously, in the same experimental situation.

Materials and Methods

Subjects

Ten experimentally-naive and drug-naive male, White Carneaux pigeons (Palmetto Pigeon Plant, Sumter, SC, USA) were used. They were housed individually in a room of constant temperature (24° C) and humidity (50%); lighting in the colony was maintained under a 12-h light-dark cycle (7:00 a.m. – 7:00 p.m.). The birds were maintained at 80–85% free-feeding body weights by restricting food intake. Water and grit were continuously available in home cages. Experimental sessions were conducted 5 days per week (Monday – Friday).

Apparatus

One BRS/LVE (Model 143-05) light- and sound-attenuated chamber was used. Three response keys (2.5 cm in diameter) were positioned 24 cm from the floor on one side of the chamber. An illuminated food magazine that could deliver mixed grain was located below the response keys (10 cm from the floor). The apparatus contained an exhaust fan that provided ventilation as well as masking noise. Experimental events were programmed and recorded by solid-state circuits in an adjoining room.

Procedure

Training. Initially, each subject was introduced to the chamber for habituation sessions. During these sessions the food magazine and magazine light were operated at random intervals. After all subjects were eating from the magazine, the following training procedure was instituted.

At the beginning of a session, the center key was illuminated by either a "bright" (0.26 footcandle) or a "dim" (0.10 footcandle) light. These intensities were determined by a Luna-Pro SBC light meter (Goessen, FRG) set at ASA 50. The intensity of the "dim" light was approximately 40% of that of the "bright" light. A peck on the center key resulted in 3-s access to mixed grain (and the magazine light). The response requirement was then increased gradually to five responses. After stable responding was established, five responses on the center key resulted in the termination of the center key light and illumination of one of the side keys. If the bright stimulus was presented on the center key, the side key was green and a single response on the green key was defined as "correct"; if the dim stimulus was presented, the side key was red and a response on the red key was correct. Responses on the correct key were reinforced with food and the magazine light. The positions of the red and green lights were alternated randomly between the left and right side keys, but occurred equally often on each key, during the 200 trial experimental session.

After responding on the center and side keys was established, differential training was begun. During this phase, five responses on the center key resulted in simultaneous illumination of both side keys, one of which was red and the other was green. Correct responses (a peck on the green key following the bright stimulus or a peck on the red key following the dim stimulus) were reinforced with mixed grain and the magazine light. A 10-s time-out period occurred after incorrect response choices. Immediately after either reinforcement or time-out, the next trial began with illumination of the center key. Subjects received 200 trials of bright or dim stimulus presentations per session in random order (100 of each); the positions (right or left) of the green and red side keys alternated randomly, but occurred equally often on each side following each discriminative stimulus. Once stable responding was again established, the probability of food reinforcement was gradually decreased to 0.30; the magazine light was illuminated on all correct-choice trials ($P = 1.0$), and served as a conditioned reinforcer. Each session continued until the animal completed 200 trials.

Drug Administration. After stable responding and choice behavior ($\geq 90\%$ correct) was established and maintained, the following drug administration procedure was instituted. Fifteen minutes prior to designated drug test sessions, each subject received an IM injection of either LSD tartrate (0.02, 0.04 or 0.08 mg/kg), morphine sulfate (2.5, 5.0 or 10.0 mg/kg) or CPZ hydrochloride (7.5, 15.0 or 30.0 mg/kg), expressed as the salt.

LSD and CPZ were prepared by dissolving the salts obtained from NIDA (Rockville, MD, USA) and Smith, Kline and French Laboratories (Philadelphia, PA, USA), respectively in 0.9% NaCl. Morphine sulfate was prepared by diluting 15 mg/ml ampules obtained from Eli Lilly and Co. (Indianapolis, IN, USA) to a concentration of 7.5 mg/ml with 0.9% NaCl. At least 3 control (no injection) days occurred before each drug test session. LSD, morphine and CPZ were given in a random order for each subject, but all doses of one drug were administered in increasing order before another drug was tested. Each dose of each drug was given to each bird once.

Data Analysis. Performance was scored for each animal for each test session and for each of the three preceding baseline (matched control) sessions. The discrimination accuracy of each bird was assessed by measures of percent correct responding on trials when the bright discriminative stimulus occurred [100 × the probability of a correct ("green") response following the bright stimulus] and percent correct on trials when the dim stimulus occurred. Position preference for each subject was assessed by measures of percent correct on trials when a left key-peck was correct (100 × the probability of a left response on trials when the correct response key occurred on the left) and percent correct on trials when a right key-peck was correct. Note that the two discrimination measures, as well as the two position preference measures, are independent of one another in that "bright" and "dim" trials, as well as "left" and "right" trials, are mutually exclusive pairs. Note also that, on half of the trials that the "bright" stimulus was presented, the correct response was on the left side-key; the same was true of "dim" stimulus trials (see Methods). Finally, response speeds for initiating trials were calculated for each subject (in responses per s) as the reciprocal of the total number of trials (200) divided by the cumulative response time for the session, where response time refers to the time between illumination of the center key light and the occurrence of the fifth peck on the center key.

Discrimination, position preference and response speed measures for the three control sessions preceding each test session were first averaged for each subject and each corresponding test session. The discrimination measures (percent correct on bright and dim stimulus trials) were subjected to a repeated measures analysis of variance (ANOVA) including corresponding drug (three conditions), dose level of each drug (three levels) and discriminative stimulus (bright vs dim) as within-subject variables. Baseline position preference measures (percent correct on the left and right side-keys) were subjected to a similar ANOVA that included corresponding drug, dose level and position (left vs right) as within-subject variables. Baseline response speeds were subjected to a repeated measures ANOVA that included drug and dose level as within-subject variables.

Because baseline discrimination performance changed over dose and time, drug data were expressed as change-from-baseline scores; i.e., mean performance of each animal on the 3 control days was subtracted from performance of that subject on the corresponding test day. In the interest of consistency, position preference and response speed measures were treated similarly. Discrimination and position preference change-from-baseline scores for each drug were subjected to separate, repeated measures ANOVAs employing dose (three levels) and bright vs dim stimuli (for discrimination) or right vs left responses (for position preference) as within-subject variables. Response speed change-from-baseline scores for each drug were subjected to separate, repeated measures ANOVAs employing dose as the within-subject variable. In addition, 95% confidence intervals based on Student's t-distribution were constructed about each mean change-from-baseline score, to determine whether or not drug administration had produced a significant (non-zero) change in performance.

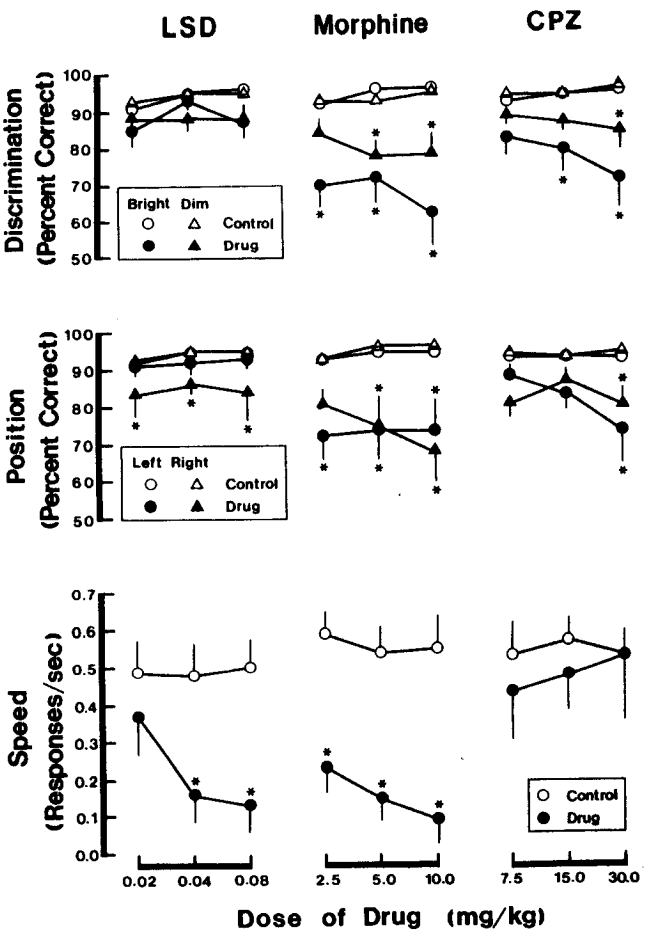

Fig. 1. Mean percent correct on bright and dim stimulus trials (top), percent correct on left and right trials (center), and mean response speed (bottom) during control sessions and following drug treatments, ± SEM ($N = 10$). For clarity, SEM bars have been omitted for all control percent correct measures; none exceeded 3.5%. $^*P < 0.05$

Results

Control Performance. Mean accuracy, position preference and response speed measures for each drug and dose and their corresponding controls are shown in Fig. 1. Baseline discrimination performance increased significantly from an overall mean of 92.7% correct to 95.4% correct with increasing dose levels of the corresponding test drugs [$F(2,18) = 9.80$, $P < 0.01$]. This effect is probably due to administering test drugs in order of increasing doses and represents a small increase in baseline discrimination accuracy over time. No other effects on discrimination performance and no interactions occurred; thus, (a) baseline performance was comparable for the three drugs and for the bright and dim discriminative stimuli, and (b) the increase in control performance over time did not differ for the three drugs or for the two discriminative stimuli.

Baseline position preference measures did not differ significantly for the three drugs, for dose levels, or for right and left responses. Control performance on both side-keys was slightly lower on control days for CPZ administration (93.1%) than for morphine or for LSD (both = 94.0%), but this difference was not statistically significant [$F(2,18) = 2.78$, $0.05 < P < 0.10$].

Baseline response speeds were slightly lower on control days for LSD (0.49 responses/s) than on those for morphine and CPZ (0.55 and 0.54 responses/s, respectively); again, this difference approached but did not reach statistical significance [$F(2,18) = 3.26$, $0.05 < P < 0.10$]. Baseline response speeds did not change over the course of the experiment and there were no interactions.

LSD. Accuracy of discrimination appeared to decrease following LSD; these changes approached but did not reach statistical significance at higher doses (Fig. 1, left top), did not differ for bright and dim stimuli, and was not dose-dependent. In addition, LSD appeared to lower accuracy of responding differentially on the right side-key (Fig. 1, left center), in that decreases in accuracy were significant following each dose for the right but not the left side-key. However, this difference was not significant when responding on the two side keys was compared directly [$F(2,18) = 1.55$, $P > 0.10$]. LSD did produce significant decreases in response speed (Fig. 1, left bottom); this effect was dose-dependent between 0.02 and 0.08 mg/kg [$F(2,18) = 4.19$, $P < 0.05$].

Morphine. One of the ten birds failed to respond within 3 h following 10 mg/kg of morphine; its matched control data for that test session were deleted from the data analyses, resulting in $N = 9$ for all performance measures following that dose of morphine. Morphine decreased accuracy on bright-stimulus trials at all three test doses and lowered accuracy on dim-

stimulus trials at the higher two doses (Fig. 1, center top). The larger effect of morphine on correct discrimination of the bright stimulus than the dim stimulus reached statistical significance [$F(1,9) = 5.05$, $P < 0.05$], although the increase in effect of morphine with increasing dose did not [$F(2,17) = 2.50$, $P > 0.10$]. Morphine lowered accuracy of responding equivalently on the left and right side-keys (Fig. 1, center) and lowered response speeds (Fig. 1, center bottom); neither of these effects differed significantly for different doses.

CPZ. CPZ also decreased discrimination accuracy for both bright and dim stimuli at higher doses (Fig. 1, right top); this effect was dose-dependent [$F(2,18) = 5.55$, $P < 0.02$]. Although CPZ, like morphine, appeared to differentially lower accuracy of responding following the bright stimulus, this difference was not statistically reliable. The effect of CPZ on accuracy was also significant for the measures of responding on both of the side-keys (Fig. 1, right center) and was again dose-dependent [$F(2,18) = 3.57$, $P < 0.05$]; no differential effect on the two side-keys was observed. Unlike LSD and morphine, CPZ did not significantly affect response speeds at any dose tested (Fig. 1, right bottom).

Discussion

The present results agree with studies showing that LSD does not affect accuracy of performing relatively simple (unidimensional) discriminations in rats or pigeons (Appel and Dykstra 1977), although it does produce dose-dependent decreases in speed of responding. They also show that this compound does not affect bias toward "bright" (or "green") or "dim" (or "red") discriminative responses, at least under conditions of high baseline accuracy. Although there are indications that LSD might alter spatial (position) bias (Fig. 1) as in previous research (Altman et al. 1979), the difference between accuracy of responding on the two side-keys was not statistically reliable; thus, the effect of LSD on this variable remains unclear. However, it is notable that all studies which have employed asymmetrical reinforcement contingencies to induce baseline response bias have shown that LSD alters this bias, although decreases (Dykstra and Appel 1974), increases (Straub and Appel 1975) or both (Altman et al. 1979) have been found. Conversely, in studies where no initial bias existed, as in the present one, no significant effect of LSD on bias was observed (Dykstra and Appel 1974; Hernandez and Appel 1979).

The present results again replicate findings that morphine decreases the ability of rats to detect various kinds of stimuli (above) and extend this observation to another species (pigeons) and another stimulus modality (brightness). Moreover, this effect is nearly maximal following the lowest dose tested (2.5 mg/kg) and is not accompanied by changes in spatial bias. Morphine did affect discrimination of bright more than dim visual stimuli but accuracies for both stimuli were decreased significantly. This result is interesting in that the discriminative stimuli employed here differed on the basis of intensity, and perception of the more intense stimulus was affected more than was perception of the less intense stimulus. Thus, morphine may affect perception generally by lowering the perceived intensity of both nociceptive and non-nociceptive stimuli. Previous studies of shock detection in rats have shown that the effect of morphine varies with stimulus intensity but, in this case, the variables are inversely related. At high shock intensities the shock vs no-shock stimuli are so distinct that no drug effect occurs; however, at lower shock intensities, morphine lowers detectability (Lloyd et al. 1978; Poling et al. 1978). Both Lloyd et al. (1978) and Poling et al. (1978) reported that this effect of morphine was significant on shock trials but not on no-shock trials. Grilly et al. (1980) also reported that morphine had a somewhat greater effect following the more intense stimulus in a shock intensity discrimination task, although the difference was not statistically significant. However, in subsequent experiments specifically designed to separate effects on shock sensitivity and response tendencies, no effect of morphine on response bias was found (Grilly 1981; Hernandez and Appel 1980). Thus, it may be that the "damping" effect on morphine on sensitivity to both noxious and non-noxious stimuli is greater for more intense stimulation. Such an intensity-dependent effect of morphine on sensitivity might explain apparent changes in bias which have been observed in some previous experiments (see Grilly 1981; Hernandez and Appel 1980 for detailed discussions of this point).

The present results also agree with findings that CPZ decreases the accuracy of visual discriminations in pigeons without affecting response bias (Altman et al. 1979; Straub and Appel 1975); they also extend these observations by demonstrating that this effect can occur in the absence of decreases in response speed (Fig. 1). Moreover, these results again show that CPZ decreases accuracy of visual discriminations in pigeons without altering (spatial) bias, although it increases "stimulus present" response bias in rats in both shock and tone detection tasks. This discrepancy may represent a species difference, a difference between visual and other types of sensory discriminations or between two-alternative detection as opposed to discrimination tasks. However, Fig. 1 suggests that changes in perceptual (brightness or color) bias, but not position preference, may occur in pigeons following CPZ under different conditions of baseline accuracy or dose range.

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