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The Effects of Hallucinogens on Blind Monkeys[1]

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Abstract. Two blind monkeys were studied with an observational profile that was previously shown to distinguish the effects of hallucinogens from those of other classes of drugs. Lysergic acid diethylamide and dimethyltryptamine could be distinguished from saline, chlorpromazine, *d*-amphetamine sulfate, and bromo-lysergic acid diethylamide by the increased frequency of spasms, stereotypy, bump, and tracking. The hallucinogens also produced dramatic increases in exploration and related behaviors normally seen only in response to real visual or auditory stimuli. These behaviors are discussed in terms of their similarity to behaviors observed with sighted monkeys in light and dark environments.

Hallucinogens induce characteristic behavioral changes in human and infrahuman primates. In man, hallucinogenic reactions are marked by states of CNS excitation and sympathetic arousal frequently accompanied by perceptual disturbances. Recent studies have indicated that hallucinogens also induce characteristic behaviors in infrahuman primates and these include an increase in the occurrence of exploration, locomotion, stereotypy, spasm, tracking, and duration of inappropriate behaviors (*Siegel et al.*, 1974; *Brewster et al.*, in press).

While the exact 'hallucinatory' nature of these changes depends on what we are willing to infer from the associated behaviors, much of the perceptual-motor behavior observed in these studies is virtually identical to that seen when the

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animal is responding to real stimuli which are physically present. For example, *Stadnicki et al.* (1974, p. 228) reported that one monkey, following cessation of chronic marihuana treatment, appeared to be hallucinating 'as evidenced by the staring at, and following of, an imaginary object with the eyes'. Similar reactions were observed in the chimpanzee by *Baldwin et al.* (1957) and in baboons by *Lagutina et al.* (1964). It has been suggested that these effects are the result of changes in attentional mechanisms (*Sharpe et al.*, 1967) and cortical responsiveness to visual stimuli (*Bermond and Bert*, 1969; *Heath*, 1973) which are projected from internal to external environments (*Dement et al.*, 1970).

Hallucinogens induce similar behavior in totally dark environments in monkeys (*Brewster et al.*, in press) and in man (*Siegel and Jarvik*, 1975). The presence of some LSD- or marihuana-induced visual imagery in totally blind subjects (*Kirtley*, 1971; *Krill et al.*, 1963), as well as non-drug-induced complex hallucinations in recently blinded subjects (*Fitzgerald*, 1971) would also seem to support the notion that drugs generate internal visual stimuli. However, adequately controlled studies with blind subjects have not been conducted and these findings must be accepted with caution (cf. *Rosenthal*, 1964).

Nonetheless, studies with blind organisms could be extremely useful in understanding reactions to any visual stimuli induced by drugs since such stimuli are not normally present for these animals. Therefore, the present investigation was conducted with two 7-year-old male *Macaca mulatta* (weighing approximately 11 kg each) who had each received a total bilateral enucleation 1 year prior to the start of the present experiment.

The normal behavior of these monkeys, Samson and Lear, was passive and uneventful relative to normal sighted monkeys. They spent most of their time sitting quietly in their home cage. Locomotion was practically non-existent except for retrieval of food. Loud sounds elicited orientation with the head and ears while unexpected stimuli, particularly those occurring close to the animal's cage (e.g., approach by a strange human), often elicited threat behaviors.

Subjects were run according to a previously described method and experimental design (*Siegel et al.*, 1974; *Brewster et al.*, in press). Briefly stated, each monkey was adapted to an observation cage located in a sound- and light-attenuated chamber and monitored via infrared television. Observers, located outside the experimental chamber, scored behavior in terms of frequency of 18 behavioral categories: locomotion, exploration (also duration), inappropriate (also duration), stereotypy, yawn, vocalization, spasm, rocking, groom, self-clasp, self-bite, fear grimace, threat, tracking, grope and bump. After several weeks of daily 1-hour adaptation sessions, drug administration was begun. Monkeys received only one drug treatment per week for 12 consecutive weeks, with regular adaptation sessions intervening between drug sessions. The drugs and doses administered were: saline (two separate sessions); chlorpromazine (CPZ), 0.5 and 1 mg/kg; bromo-lysergic acid diethylamide (BOL), 100 μg/kg; LSD, 50

Table I. Mean behavior scores for each drug condition

Behavior	Base-line	Saline 1	Saline 2	CPZ, mg/kg		BOL 100	LSD, μg/kg		DMT, mg/kg				
				0.5	1	μg/kg	50	100	0.5	1	2	3	4
Locomotion	0.0	0.0	0.0	2.8	8.1	1.0	0.9	1.6	0.3	0.0	0.0	0.4	1.4
Exploration	34.6	27.6	20.4	33.5	25.4	59.8	134.9	119.1	31.1	32.6	86.6	70.0	213.9
Inappropriate	0.0	0.0	0.0	0.4	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Stereotypy	0.0	0.0	0.0	0.0	0.0	0.0	0.0	17.1	0.0	0.0	0.0	0.0	3.6
Yawn	0.0	0.0	0.0	0.0	0.6	0.0	9.6	1.3	0.3	0.0	5.3	0.3	5.5
Vocalization	0.1	0.0	0.0	0.1	0.1	0.1	30.1	1.1	0.3	0.0	7.4	0.1	1.4
Spasm	0.0	0.0	0.0	0.0	0.0	0.0	15.4	59.9	0.0	0.0	9.9	14.1	6.9
Rocking	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.5	0.0	0.0	0.3	0.0	0.0
Groom	0.0	0.0	0.0	0.0	0.1	2.3	2.0	0.1	0.0	0.0	0.5	0.0	0.0
Self-clasp	0.0	0.0	0.0	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Self-bite	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Fear grimace	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Threat	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tracking	0.0	0.0	0.0	0.0	0.0	0.0	6.9	1.0	0.0	0.0	0.6	0.1	14.3
Grope	0.0	0.1	0.0	0.0	0.5	1.3	0.1	0.6	0.4	0.0	0.0	0.9	0.9
Bump	0.0	0.0	0.0	0.0	0.0	0.0	1.9	0.0	0.0	0.0	0.0	0.0	1.5
Inapp. clock, sec	0.00	0.00	0.00	90.35	332.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Explor. clock, sec	0.00	0.00	0.00	0.00	1.33	5.23	103.06	24.11	0.00	0.00	0.00	22.43	14.21

and 100 μg/kg; dimethyltryptamine (DMT), 0.5, 1, 2, 3, and 4 mg/kg. All drugs were administered intramuscularly in a constant volume of 0.1 ml/kg saline. *d*-Amphetamine sulfate, used in previous studies with sighted monkeys, was not employed here after Lear died in this study after receiving 2 mg/kg. All drug treatments were administered in a random sequence. In the experimental sessions, each animal was injected and behavior during the 60 min following injection was observed and scored independently by two observers without knowledge of the drug treatment. Since Lear had only received one dose of saline, CPZ, *d*-amphetamine, and DMT prior to his death, his data are discussed separately.

Table I presents the mean number of occurrences and clock time (in seconds) of each behavior for each drug dosage, averaged for both observers' scores for Samson. Here it can be seen that hallucinogens could be distinguished from other drug treatments by the increased frequency of spasms, stereotypy, bump, and tracking. A dramatic increase in exploration behavior was also apparent with LSD and DMT. However, clear dose-response curves were not obtained with this single animal, although frequency of exploration did show some quantitative variation with dose of DMT.

The results for Lear were basically in agreement with those found for Samson. DMT (2 mg/kg) could be distinguished from saline and CPZ (1 mg/kg) by the increased frequency of spasm, stereotypy, bump, tracking, locomotion and exploration. *d*-Amphetamine (2 mg/kg) also increased these behaviors, but since Lear died within 2 h following this dose, this result cannot be adequately interpreted. These results can be compared to those obtained with sighted monkeys in previous studies. Hallucinogens increased the frequency of spasms and stereotypy in sighted animals and such increases appeared clearer in dark environments. Samson and Lear displayed similar increases with hallucinogens here. In addition, these animals' rather low baseline levels of normal behavior may have allowed for the emergence of other hallucinogen-specific responses. These latter behaviors included tracking, exploration and bumping into the cage (usually while locomoting). Samson and Lear, unlike the sighted monkeys, manifested increased vocalizations during hallucinogen sessions. These latter responses included chewing and licking and are components of the oral syndrome observed in mescaline-treated monkeys and sometimes labeled 'somatosensory hallucinations' (*Klüver*, 1966).

Perhaps the most dramatic behavior was that observed with 50 μg/kg LSD, which was Samson's first hallucinogen treatment. 5 min following injection, Samson reached for his eye sockets – a response never before observed in this animal – and started rubbing them while shaking his head and periodically 'freezing' in a crouched and attentive posture, a posture characteristically observed in monkeys following treatment with active cannabinoids (*Grunfeld and Edery*, 1969). This cycle of behavior was repeated four more times over the next

10 min, the eye-socket rubbing being carried out with the right and then the left hand. The concomitant increases in bumps and exploration of the cage walls with directed hand and mouth movements prompted the inference that this was a startle response to a visual stimulus. Other changes in behavior support this interpretation. Samson's normal reaction to stimuli consisted of rapid head- and ear-orienting responses followed by head turning and swaying 'as if' searching for the location of the sound. These behaviors increased dramatically during hallucinogen sessions. Seemingly, accidental tactile encounters with the cage environment would elicit increased exploration with the hands and the head- and ear-orienting responses. Lear, following DMT (2 mg/kg) executed numerous 'startle-like' reactions coupled with tracking movements. In one sequence, Lear repeatedly stood up and sat down, 'looking' or orienting around the cage, while periodically jerking and moving backwards 'as if' startled. One such startle reaction was accompanied by a fear grimace. These patterns of behavior are consistent with the dominance of auditory responses in blind children and their pattern of searching the environment for the location of a sound (*Fraiberg et al.*, 1966: *Schlaegel*, 1953) as well as with facial expressions of blind monkeys (*Berkson and Becker*, 1975). Indeed, *Forrer and Goldner* (1951) report that two blind humans treated with LSD (1 μg/kg) did not have visual hallucinations but may have misinterpreted stimuli in other modalities and experienced olfactory hallucinations.

It may be speculated that the type of exploration, tracking and groping behavior seen here constitutes a motor attempt by the organism to verify perceptions. In man, hallucinogenic and hallucinatory states have been associated with changes in perceptual constancies and some psychophysical judgments which interfere with the ability to validate such sensory information (*Fischer*, 1971). In monkeys, variable changes in psychophysical judgments with some hallucinogens have also been found (*Brown and Bass*, 1967). Thus, Samson's exploration, tracking and groping behaviors may represent motor responses to changes and variations in perceptual systems. Such behaviors are strikingly similar to those of pre-verbal children given the hallucinogenic anesthetic ketamine prior to surgical procedures (*Siegel and Jarvik*, 1975). The mechanism of action responsible for such effects is largely unknown but may be related to recent studies in cats which found that hallucinogens like LSD and DMT 'mimic' the effect of light on the retina (*Heiss et al.*, 1973) or on EEG tracings (*Marczynski*, 1972). Such drugs 'might be interpreted by the brain as light and this may contribute to the origin of abnormal reactions within brain structures which are also influenced, leading to hallucinations' (*Heiss et al.*, 1973, p. 457). While more work is needed with blind and sighted subjects in order to confirm this hypothesis, including testing of subjects prior to blinding, the effects of hallucinogens on blind and sighted monkeys appear very similar, and are therefore primarily related to central rather than peripheral processes.

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