Psychological Reports, 1969, 25, 704-706. © Psychological Reports 1969

PSYCHEDELIC-INDUCED SOCIAL BEHAVIOR IN MICE: A PRELIMINARY REPORT[1]

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Summary.—When large populations of mice were treated with LSD (2mcg/kg to 30mcg/kg), bufotenine (5mg/kg to 30mg/kg), a cannabis sativa extract (50mg/kg to 100mg/kg), or tetrahydrocannabinol (2mg/kg to 10mg/kg), there was a dramatic change in social behavior. Such treatment produced a significant reduction in aggression, group aggregation, and temporary disruptions of social hierarchies. Hallucinogenic-treated mice placed in normal untreated colonies were hypersensitive to auditory and tactile stimulation and aggregated in small groups apart from the rest of the population. Treatment with saline or BOL-148 produced no significant changes in behavior.

Typically, low doses of psychedelics (lysergic acid diethylamide, mescaline, cannabis sativa, and tetrahydrocannabinols) lower spontaneous activity in rodents and induce hypothermia, hypersensitivity, and ataxia. Higher doses usually reduce activity markedly and induce sedation. These effects have been reviewed in detail elsewhere (Hoffer & Osmond, 1967; Holtzman, Lovell, Jaffe, & Freedman, 1969). There is also evidence that psychedelics diminish aggressiveness and fighting behavior in mice (Uyeno & Benson, 1965; Santos, Sampaio, Fernandes, & Carlini, 1966; Silverman, 1966; Uyeno, 1966b) and inhibit dominance behavior of rats competing for food (Uyeno, 1966a). In these studies, *E*s have been concerned primarily with the behavior of small groups of mice ($n =$ 2 to 4). Less attention has been given to the study of these effects in large populations of animals. This paper is a preliminary report of several experiments carried out on the effects of psychedelics on the social behavior of large populations of laboratory mice.

Large populations of 40 to 50 mature CF1 male mice (Carworth) were reared together in wire mesh cages (36 in. × 36 in. × 18 in.). They were provided with free access to food and water. Each mouse was numbered with a Carbol Fuchsin stain on his back so observers could readily identify him. Such colonies engage in characteristic patterns of behavior. The mice spend about 60% of the time of observation in aggregation as measured by the criterion of being within a body-length of another mouse. Usually the more dominant mice would be dispersed or separated from the others. Dominant mice tended to feed first and would often establish territories and defend these against intruders. Such relationships were stable for 3 or 4 days at which time major fights would establish new social hierarchies. In general, at least 45 distinct social postures

[1]Supported in part by a grant from the Dalhousie Medical Faculty Research Fund.
[2]RKS served as licensed investigator. The authors are indebted to Dr. Mark Segal for advice and support.

could be observed (cf. Grant & Mackintosh, 1963). Double-blind observers scored each mouse in each colony on all 45 postures. During each daily observation period the frequency of occurrence of the social posture was recorded for each mouse along with the identity of the other animals interacted with.

Initially, normal mice from other colonies (strangers) were introduced into the experimental populations. These strangers would be sniffed, nosed, licked, and otherwise investigated by the colony inhabitants. Occasionally these strangers would be attacked by dominant mice but usually they were rapidly assimilated into colony activity. However, if these strangers were injected with either lysergic acid diethylamide (LSD: 2mcg/kg to 30mcg/kg i.p.), bufotenine (5mg/kg to 30mg/kg i.p.), a cannabis sativa extract (marihuana: 50mg/kg to 100mg/kg i.p.), or Δ^9-tetrahydrocannabinol (THC: 2mg/kg to 10mg/kg i.p.), they appeared hypersensitive.[3] Each time they were approached by colony inhabitants they would squeal, squeak, and retreat from the investigation. If attacked by a dominant inhabitant they would not fight back and this failure to assume an aggressive posture would usually discourage and terminate the attack. Injected mice would exhibit head-twitches (cf. Corne & Pickering, 1967), ataxia, and hypothermia (2 to 3°C). Grooming movements would be rapid and longer in duration than usual. The injected mice would try to move into areas of the colony where they would not be investigated by the inhabitants. However, the ataxia associated with such movement would usually just increase physical contact with others who further investigated and attacked these strangers. Eventually, some of the drugged strangers would come in contact with other drugged mice. These mice would not try to investigate each other and, since the animals were in hypothermia, they would aggregate with each other for warmth and the usual aggregation motivation of mice. This aggregation would last for 6 to 8 hr. When strangers were treated with either saline or bromolysergic acid diethylamide[4] (BOL-148: 2mcg/kg to 30mcg/kg i.p.), they behaved normally and were rapidly assimilated into activity of the colony.

For assessment of psychedelic effects on the entire populations, solutions of either LSD or bufotenine were prepared and added to the water supplies of the colonies. The solutions had previously been calculated to supply each mouse in the colonies with an hallucinogenic dose within 6 hr. of normal drinking behavior. At that time observations were begun. The most dramatic effect was that colony inhabitants were completely dispersed with no more than 2% of the mice in aggregation. When mice moved across the cage area they tended to avoid contact with others. Mice would frequently hop in the air in retreating

[3]LSD was obtained from Sandoz Ltd., Basle, Switzerland; bufotenine from Upjohn Co., Kalamazoo, Michigan; cannabis and THC from Division of Narcotic Drugs, United Nations Office at Geneva, Switzerland. Cannabis extract prepared according to Carlini and Kramer (1965).

[4]BOL obtained from Sandoz Ltd., Basle, Switzerland. BOL is identical to LSD in its antiserotonin and peripheral effects but lacks any central hallucinogenic activity.

from approaching mice. Any given fight in any part of the colony would often incite the entire colony into a short burst of disoriented activity. As the drug effect developed, activity was more diminished. If a fight did occur it was of significantly shorter duration than normal fights and never involved actual physical injury. When a fight did occur, nearby mice, who normally showed little concern, would often retreat from the fight area or exhibit tail-rattles. Grooming behavior was rapid and head-twitches occurred frequently for most mice. Dominance relationships and territories remained stable throughout the drug exposure and afterwards. All social postures, when they did occur, appeared normal.

Since cannabis and THC are insoluble in water, the mice in the colonies had to be individually injected with ethanol solutions of the cannabis extract and the THC in order to assess these drugs. Behavior was essentially similar to that observed under treatment with LSD and bufotenine. However, the cannabis extract had a large sedative effect which suppressed most activity. Treatment with BOL-148, saline, and ethanol in the water supplies did not significantly alter behavior from normal.

When strangers were introduced into the drugged colonies, they were relatively ignored by the inhabitants. This was true whether the strangers were introduced in a drugged or undrugged state. If the strangers were undrugged, however, they moved about the colony investigating mice and inducing squealing and flight behavior in the inhabitants. And, if the strangers were dominant mice to begin with, they would often establish dominance over the entire colony, exploiting the food supplies and territories of the inhabitants.

REFERENCES

CARLINI, E. A., & KRAMER, C. Effects of cannabis sativa (marihuana) on maze performance of the rat. *Psychopharmacologia (Berl.)*, 1965, 7, 175-181.

CORNE, S. J., & PICKERING, R. W. A possible correlation between drug-induced hallucinations in man and a behavioural response in mice. *Psychopharmacologia (Berl.)*, 1967, 11, 65-78.

GRANT, E. C., & MACKINTOSH, J. H. A comparison of the social postures of some common laboratory rodents. *Behaviour*, 1963, 21, 246-259.

HOFFER, A., & OSMOND, H. *The hallucinogens*. New York: Academic Press, 1967.

HOLTZMAN, D., LOVELL, R. A., JAFFE, J. H., & FREEDMAN, D. X. 1-Δ^9-tetrahydrocannabinol: neurochemical and behavioral effects in the mouse. *Science*, 1969, 163, 1464-1467.

SANTOS, M., SAMPAIO, M. R. P., FERNANDES, N. S., & CARLINI, E. A. Effects of cannabis sativa (marihuana) on the fighting behavior of mice. *Psychopharmacologia (Berl.)*, 1966, 8, 437-444.

SILVERMAN, A. P. The social behaviour of laboratory rats and the action of chlorpromazine and other drugs. *Behaviour*, 1966, 27, 1-39.

UYENO, E. T. Effects of d-lysergic acid diethylamide and 2-bromlysergic acid diethylamide on dominance behavior of the rat. *International Journal of Neuropharmacology*, 1966, 5, 317-322. (a)

UYENO, E. T. Inhibition of isolation-induced attack behavior of mice by drugs. *Journal of Pharmaceutical Sciences*, 1966, 55, 215-216. (b)

UYENO, E. T., & BENSON, W. M. Effects of lysergic acid diethylamide on attack behavior of male albino mice. *Psychopharmacologia (Berl.)*, 1965, 7, 20-26.

Accepted September 15, 1969.