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# THE MATURATIONAL EFFECTS OF LSD UPON BRAIN WEIGHT AND BEHAVIOR IN THE MOUSE

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ABSTRACT

1. Mice exposed to LSD on day 1 or day 7 post-partum showed no altered exploratory behavior when tested by the ' head poke ' test at 8 weeks post-partum.

2. Male mice exposed to LSD (5·0 and 50·0 μg./kg.) on day 1 post-partum showed reduced brain weight in some regions of the brain when measured at 8 weeks post-partum. Male mice exposed to LSD on day 7 and female mice exposed on day 1 or day 7 showed no such weight change.

THE POSSIBILITY of birth defect induction by lysergic acid diethylamide (LSD) was first raised in 1967 (Alexander, Miles, Gold & Alexander, 1967). Since then a body of essentially conflicting data has been accumulated and recent reviews of all reports arrive at much the same conclusion: the evidence for LSD-induced developmental abnormality is not convincing (Dishotsky, Loughman, Moger & Lipscomb, 1971; Long, 1972; Kalter, 1972). The focus of most of these studies has been upon gross physical deformity caused by LSD exposure during the period of prenatal development. We have investigated the effects of LSD upon the mouse during the period of maturation, and have considered alterations in behavior and brain weight.

## MATERIALS AND METHODS

Exploratory behavior and weights of brain parts in CFW mice given single intraperitoneal injections of LSD on either 1 or 7 days post-partum were measured. These days were chosen for drug exposure as they represent the start of postnatal life or the mid-period of the very rapid brain growth phase which extends through the first 2 weeks post-partum (Baker & Hoff, 1972). The behavioral test employed here has been effectively used to measure LSD effect in adult rats (Voss & Berger, 1972). The drug doses used were 0·5, 5·0 and 50·0 μg./kg.; control animals were injected with the carrier only. Animals were allowed to grow to maturity and tested at 8 weeks. Behavior was tested using the ' head poke ' test. Mice were placed on a board in which 16 holes were drilled. They were scored for the number of times they ' poked ' their head into a hole during 2 minutes. All mice were run twice through this test. Brain weights were taken from freshly-killed mice. The brain was subdivided into four parts including the cerebellum, cerebral hemispheres, a mesencephalon–diencephalon fraction and a medulla-pons fraction. The specific method of dissection has been previously described (Baker & Hoff, 1972).

## RESULTS

The ' head poke ' test showed no significant differences between control and LSD injected mice of both sexes. As seen in Table I there is a significant reduction in brain weight for male animals injected on day 1. Hemispheres and mescephalon–diencephalon showed a significant reduction only at the 50·0 μg./kg. dose, and medulla-pons showed reduced weight at the 5·0 and 50·0 μg./kg. dose with the greatest reduction at the highest dosage. There was no brain weight change in any males injected on day 7, or any females injected on either day.

## DISCUSSION

Although a reduction in brain weight is found in day 1-injected mice there is no behavioral change in any of the mice we studied. We conclude that either there is no long-term drug effect upon this behavioral complex, or that the method of testing lacks

Table I.—Brain Region Wet Weights in Milligrams of Male Mice 8 Weeks Post-partum after LSD Exposure on 1 Day Post-partum

| | Hemispheres | Mesencephalon–Diencephalon | Medulla Pons |
|---|---|---|---|
| Control | | | |
| $N$ = | 33 | 33 | 33 |
| $X$ = | 262·5 | 85·4 | 59·7 |
| S.E.M = | 1·93 | 0·80 | 0·70 |
| 5·0 μg./kg. LSD Dose | | | |
| $N$ = | 36 | 35 | 35 |
| $X$ = | 259·4 | 84·1 | 57·3 |
| S.E.M = | 1·42 | 0·74 | 0·59 |
| $P$ = | N.S. | N.S. | < 0·02 |
| 50 μg./kg. LSD Dose | | | |
| $N$ = | 25 | 25 | 25 |
| $X$ = | 253·5 | 82·7 | 56·5 |
| S.E.M = | 2·65 | 1·02 | 0·77 |
| $P$ = | < 0·01 | < 0·05 | < 0·01 |

$N$ = number in sample; $X$ = mean value; S.E.M = standard error of the mean; $P$ = probability of differences from controls derived from Student's $t$-test; N.S. = not significant.

the necessary resolution for discovering such an effect.

Specifying the reason for brain weight reduction is difficult. The most-studied effects of LSD is its antagonistic action on the function of serotonergic neurons in the brain, despite the fact that the nature of such action is still obscure (Aghajanian, 1972). A number of drugs that interact with the biochemistry of the brain's serotonergic neurons have also been shown to cause a reduction in brain growth when applied to immature rats (Hole, 1972a, b). In some cases these experiments have produced behavioral alterations as well, which were not found in our experiments. Not all such serotonin interacting drugs are able to retard brain growth (Hole, 1972c), and a sexual dichotomy of effect, such as we have observed, is not reported. Another possible mechanism may be operative, since a general effect of LSD upon brain cell lysosomal systems resulting in abberant cytology was reported by Hendelman (1972). Neither of these possible actions would, however, account for the sexual difference observed in our experiments. Since the time of effective exposure is day 1 and the sex affected is male, the special situation of the male neonate is probably critical. The most obvious relationship is the residual level of prenatal androgen present following birth (Miyachi, Nieschlag & Lipsett, 1973).

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*Key Word Index*: Lysergic acid diethylamide, LSD, mouse, brain, behavior.