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liver mitochondria from deficient rats; EDTA, however, prevented only the swelling of liver mitochondria. Mitochondria of heart contained twice the amount of magnesium found in liver mitochondria. The mechanism of decrease of P/O ratio of mitochondria from magnesium deficient rats and the physiological significance of magnesium deficiency induced swelling of mitochondria, were discussed.

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## Effects of LSD-25 on Food Intake in the Rat.* (26925)

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In an earlier study(1) of certain similarities between the effects of LSD-25 and amphetamine sulfate, a depression of body weight was observed in rats injected daily with 0.50 mg/kg of LSD-25. It seemed logical to suppose that this was the result of depression of food intake since Winter and Flataker(2) reported that at the height of the drug effect their rats did not eat. The present work quantifies this effect of LSD-25 and investigates the possibility of development of tolerance to daily doses of the drug.

*Method and results. Experiment I.* Thirty-six male albino rats of the Sprague-Dawley strain were trained for 18 days to feed 2 hours a day (2-4 p. m.) on powdered Purina Lab Chow. At the end of this period their mean body weight of 246 ± 3 g was approximately 80% of normal and they were assigned to one of 4 groups on the basis of mean amount of food intake over the last 3 training days. (Mean weights of the 4 groups did not differ significantly). Just before 2 p.m. on the 19th day, one of each of 3 groups was injected IP with one of the following doses of LSD-25: 0.13, 0.26, or 0.52 mg/kg. (LSD-25 was dissolved in Ringer's solution and doses prepared so that all animals received the same amount of fluid in proportion to body weight). The fourth group was injected with a comparable amount of Ringer's solution alone. Immediately after injection the animals were returned to their living cage, given cups of chow, and permitted to feed 2 hours. Four days of no injections and 2-hour feeding followed. On the fifth day each animal was again injected with the same dose level and permitted to feed 1½ hours. After another no-injection, 4-day interval with 2-hour feeding, the animals were again injected with the same doses and permitted to feed for one hour.

The data of this study (Fig. 1), show a depression of food intake as a function of LSD-25 dosage. A repeated measures analysis of variance(3) was run using the data of all 4 groups over the 3 injection days. This analysis yielded the following F ratios: be-

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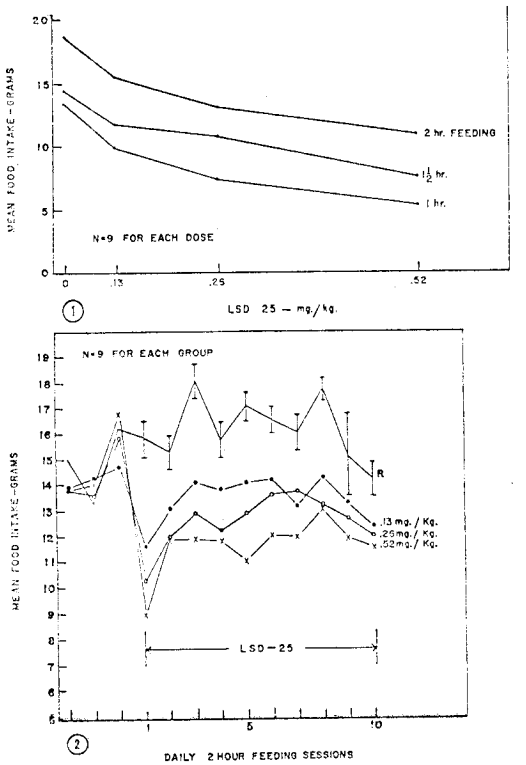


FIG. 1. Food intake as a function of LSD-25 and time allowed to feed.

FIG. 2. Mean food intake (2-hr feeding) with daily inj. of LSD-25. Stand. error of means has been plotted for the Ringer's group.

tween methods = 68.5; between trials = 69.9; and interaction, trials and methods = 0.70. The first 2 were significant beyond the .01 level while the latter was not significant. These data reveal significant differences between dosage levels and time allowed to feed, but no differences between the shape of the curves generated by these 2 variables. The equation of the log dose relationship determined by analysis of the data for the first injection day (2-hour feeding) was, $Y = 16.2 + 7.5 \log X$.

*Experiment II.* In this study 36 male rats of the same strain were trained on the 2-hour, powdered chow feeding schedule for 14 days prior to first injection. On the first injection day these animals had a mean weght of 245 ± 4 g and were approximately 80% of normal body weght. Four groups were formed on the basis of mean food intake over the last 3 days of the training period (Mean weights of the 4 groups did not differ significantly). The same dosage levels of LSD-25 as used in Exp. I were investigated. Procedures were identical except that in this work all animals were injected and tested daily for 2 hours of feeding at 24-hour intervals for 10 days. These tests were run to determine whether or not the experimental groups would show a resumption of food intake at the level of the control group.

The results of this study (Fig. 2) show a drop in food intake with injection of LSD-25. A repeated measures analysis of variance of the 4 groups over the 10 injection days yielded the following F ratios: between methods = 7.43; between trials = 9.26; and interaction, trials and methods = 2.40. All of these ratios were significant beyond the .01 level. The between trials F appears to be related to the large increase in food intake in the experimental groups on the second injection day. Even so, none of the drug groups reached the control level at any period during the 10 days.

*Discussion.* These results show a log dose relationship between LSD-25 and depression of food intake but tolerance effects are not so obvious. A complete tolerance, in the sense that the experimental groups were back at the control level after 10 days, was obviously not obtained. Tolerance in the classical sense and defined as, "a phenomenon characterized by the fact that more and more of a drug must be used to produce equivalent effects"(4), was investigated only indirectly. For example, if tolerance developed over the 10 days of drug injection food intake of the experimental groups should have increased gradually, since dosage levels remained constant. In fact, the design of the study was such that it would tend to enhance any tolerance effects. As the groups given the drug were eating less than the controls they were becoming more deprived; this could have interacted with the drug effect to produce greater food intake in the drug groups. On the second day such an increase occurred, but the lack of any further increase contradicts such an interpretation. In fact, it was not until 5 days after the last injection (with the

animals still on the 2-hour schedule but without injections) that the drug groups were eating as much as the controls. Whether this phenomenon was a direct, prolonged, drug effect, or the result of conditioned suppression of food intake, is not known. Conditioning could have occurred through pairing of the injection with presentation of food. This is an interesting hypothesis and one worth further investigation.

In previous work(1) investigating similarities between LSD-25 and amphetamine, rats injected with these substances showed increased speed in running to escape shock and increased incidence of avoidance of shock. The present work demonstrates still another similarity between the 2 drugs, although amphetamine was not investigated here since its anorexic effects are well known.

These present studies indicate that for assay of LSD-25, food intake is a reliable and sufficient dependent variable. They also serve as a warning on the use of food reinforcement in psychological testing of drug effects.

*Summary.* Suppression of food intake in the rat was shown to follow injection of LSD-25 and this effect was determined to be dose dependent. When the effects of 10 daily injections of the drug were investigated, a suppression of food intake on each day indicated a lack of development of complete tolerance. These data show that caution is needed in interpretation of the behavioral effects of LSD-25 where such behavior is dependent upon food reinforcement.

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## The Zinc Content of Rat Sperm Cells from Ejaculate, Vas, Epididymis and Testis.* (26926)

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No biological role is known for the high concentrations of zinc in many tissues of the male mammalian reproductive tract, including human prostate(1), ejaculate(2) and sperm cells(3), canine prostate(4) and prostatic fluid(5), rat dorsolateral prostate and rabbit prostate(6). By mating male rats after ligation of the dorsolateral prostate, Gunn and Gould(7) showed that the zinc normally released by this gland is not needed for rat fertility or fecundity. If prostatic fluid were the sole source of zinc in the rat ejaculate, their data would virtually rule out a role for (male) zinc in rat fertilization. However, Wetterdal's data(8) suggest that there is another source of zinc. After injecting zinc-65 into rats he found high activity in the testes and an activity peak which traveled through the sperm transport system along with the spermatozoa that had been maturing in the testes at time of injection. A high concentration of zinc in rat sperm cells, independent of the prostatic fluid, is confirmed in the present paper by direct measurements on spermatozoa taken from ejaculates, vas, caudal epididymis and testis.

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