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Effects of LSD on Open Field Performance in Rats

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Summary. LSD has been reported to have variable actions on locomotor and exploratory activity in rats. In the present study LSD in doses ranging from 2 to 500 µg/kg induced varying effects on different components of Open Field behaviour. The "ambulation score" showed a linear increase with increasing log doses while the highest dose caused a steep rise. The "rearing" and "preening scores" exhibited an inverted U type dose-response relationship, the inversion of the curve occurring with doses higher than 8 µg/kg. It is suggested that LSD in normal doses increases all stereotyped activity whereas with higher doses only simple stereotyped activity is increased. Simple horizontal stereotyped activity therefore increases at the cost of vertical stereotype. Thus LSD increases stereotyped activity with increasing dose but while normal doses increase both the horizontal and the vertical type of activity, the higher doses increase only the horizontal type.

Key-Words: LSD — Open Field Test.

Introduction

Lysergic acid diethylamide (LSD) has been shown to induce pronounced excitation (TAESCHLER, 1960) and to increase locomotor activity (HAMILTON, 1960) which tends to confusion and violent head shaking (WINTER and FLATAKER, 1957). In rats, however, the drug impair conditioned avoidance response (COOK and WEIDLEY, 1957; JARRARD, 1963). Some of these findings appear to contradict each other, as ambulation or locomotor activity may be a pre-requisite for the acquisition and maintenance of a conditioned avoidance response (GUPTA, 1967).

Much of the inconsistency in the results, due to the effects of LSD on stress-induced behaviour of rats, seems to arise from the lack of a common terminology to describe the stressed behaviour and also from a neglect of the constitutional determinants of individual differences in the performance. These constitutional determinants of behaviour may be "reactivity" or "activation" (HOLLAND and GUPTA, 1966) or "pre-

disposition to stereotypy" (RANDRUP and MUNKVAD, 1968). The differences in "reactivity" have been shown to stem from functional differences in the autonomic nervous system (GUPTA, 1967). The differences in "activation" have been shown to arise from the functional differences in central nervous system mechanisms (LAT, 1963), predominantly those of reticular formation (EYSENCK, 1957). The differences in "predisposition to stereotypy" seem to emerge from the functional differences in neural mechanisms related to the corpus striatum (RANDRUP and MUNKVAD, 1968). BROADHURST (1960) has reported that, among other responses, a lack of ambulation in rats subjected to a stressful situation in the "Open Field Test", is a measure on which individual differences can successfully be ascribed to the differences in "reactivity" or emotionality of the subject. Similarly, LAT (1965) has shown that rearing response in rats is a behavioural correlate of "activation" or non-specific tonus of the central nervous system and rats bred selectively for high and low rearing performance for several generations are found to produce significant strain differences on several measures of locomotor activity. Moreover BLEULER (1961) has indicated that a stereotyped response may be one of the behavioral measures of psychoticism.

On the assumption that the type of stress given in the "Open Field Test" situation may induce behaviour, the components of which may be representative of "activation", "reactivity" and stereotypy, several components of the behaviour of rats in the "Open Field Test" were studied under the effect of different doses of LSD.

Methods

Subject. The subjects were naive male albino rats of Haffkine's strain weighing between 100 to 150 g. No attempt was made to control their early environment; temperature, lighting, handling etc., were allowed to vary in an attempt to obtain a heterogeneous population.

Apparatus. The apparatus (Fig.1) used for the "Open Field Test" was similar to that used by HOLLAND and GUPTA (1966). Briefly, it consisted of a circular open arena made up of wood measuring $32\frac{3}{4}$ inches in diameter, enclosed by a sunmica wall $12\frac{1}{2}$ inches high. The floor, which had a sunmica surface, was marked out in three concentric circles divided into segments by lines radiating from the floor centre. The wall was fixed on the outermost of these circles. The markings provided 25 floor units of approximately equal size and were used to score the ambulation of the animal moving around in the arena during the test. The placement by the rat of all four of its limbs in a segment was taken as one unit of ambulation. In the "Open Field Test" two types of stimuli were presented to the animal: white noise with an intensity of 78 dB

Fig.1. Open field test apparatus. The arena was marked out in three concentric circles.

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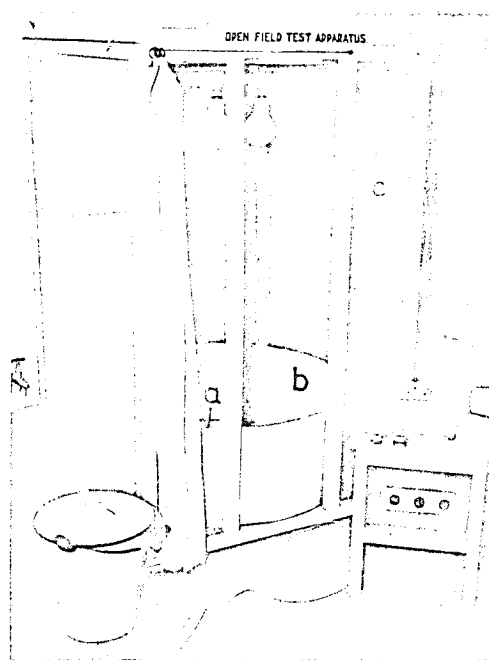


Fig. 1. Open field apparatus. a) Circular open arena made up of wood measuring $32\frac{3}{4}$ inches in diameter enclosed by a sunmica wall. b) $12\frac{1}{2}$ inches high. The floor was marked out in three concentric circles divided into 25 floor units. A translucent glass screen. c) Enclosed the arena from all sides

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was presented by an oscillator through 5 loudspeakers, and light of 165 foot candles intensity was produced by five photographic lamps. A translucent glass screen enclosed the arena from all the sides, the front side having a glass door through which the subject was placed in the arena and the experimenter observed the rat under test. By the side of the arena there was a small table on which three hand-operated counters were fixed to record the number of ambulation, rearing and preening responses. There was a clock on the table for recording the testing period. The ambulation response was defined as a "walking around" score derived from the number of radial segments of the arena which were crossed by the subject. Rearing response was defined by the number of times the rat stood on its hind legs during the test. Preening response was determined by the number of times the animal scratched his face by his forearms.

Design. An experimental design composed of six cells was employed in the present experiment; each cell contained five rats. Thus in all

Table 2. Ambulation scores in "Open Field Test". *t*-test Table for the LSD dose group mean differences F -ratio = 7.87 with 4 and 20 df. sig. 1%. Each dose group was composed of 5 rats. The response due to five different doses of the drug was compared with one another. The relevant *t* value between any pair of doses is given against that pair. For example, in column 3, 1.64 is the *t* value between the response of the third and the first dose and 0.87 between the responses of the third and second dose

Dose group	2	3	4	5
1	0.80	1.64	1.93	5.23 ^a
2		0.87	1.09	4.38 ^a
3			0.30	3.60 ^a
4				3.30 ^a

^a P 0.01.

Table 3. Rearing score in O/F. *t*-test table for the LSD dose group mean difference F -ratio = 7.30 with 4 and 20 df. sig. 1%. Each dose group is composed of 5 rats. The response due to five different doses of the drug was compared with one another. The relevant value between any pair of doses is given against that pair. For example, 0.19 is the *t* value between the responses of the third and the first dose and 1.70 between the responses due to the third and the second dose

Dose group	2	3	4	5
1	1.50	0.19	2.00 ^a	3.40 ^b
2		1.70	3.50 ^b	4.90 ^b
3			1.80	3.20 ^b
4				1.40

^a P 0.05; ^b P 0.01.

Discussion

The results obtained on the "ambulation" score indicated a general dose-effect of LSD, outlining a progressive facilitation of locomotor activity which increased as the dose rose from 2 µg/kg to the highest dose of 500 µg/kg. These results are consistent with those reported by other workers, who have studied the effect of several doses of CNS-stimulant drugs on locomotor activity in rats (BROADHURST *et al.*, 1959; LAT, 1965). They suggest that a higher "ambulation" score in the "Open Field Test" may not only be determined by the non-emotionality of the rat as has been suggested by BROADHURST (1960) but also by a higher level of CNS-excitation which is a function of CNS-stimulant drugs (LAT, 1965).

LSD has been shown to induce psychotic symptoms (MURPHREE, 1962) and psychotic patients may exhibit stereotyped behaviour e.g. moving in the same circle in a garden (BLEULER, 1961). Although there is no evidence bearing upon the implications of these observations for rat-behaviour. LAT (1965) has reported several types of stereotyped responses in rats when subjected to an unavoidable stressful situation

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under the effect of amphetamine. Thus, translating the findings reported by LAT (1965) into the Open Field terminology, it can be argued that any response can become stereotyped provided that it is exhibited continuously, vigorously and purposelessly in a fixed pattern. In the present study it was observed that rats given increasing doses of LSD, exhibited an increasing ambulation in the outermost circle in contrast to those animals that were treated with only placebo. The latter group of animals ambulated in more or less every area of the arena in order to explore the situation with the aim of escaping; for this purpose they made other intermittent response like rearing on the walls of the arena. The implication of these findings is that stereotyped behaviour in the "Open Field Test", which is a function of LSD, is characterised by irrelevant ambulation. On the other hand, emotional behaviour in the "Open Field Test" should be characterised by lack of exploratory behaviour; the animal being frozen in such a stressful situation. With this explanation it would be expected that increasing doses of LSD would produce an increasing rate of ambulation in the fixed pattern of vigorous movement in the outermost circle of the open field arena. The results obtained in this study confirmed to this expectation which is supported by the results obtained from the analysis of "rearing" and "preening" scores of the same rats.

Although the total variance produced by the dosage was highly significant on the rearing performance, the first three doses having failed to differ from each other at an acceptable level of significance. It was only the last two doses (132 and 500 $\mu\text{g}/\text{kg}$) which decreased rearing. The fact, that the response to LSD was different from that of amphetamine, further indicates the difference between the LSD-induced hallucinatory effect of reducing the rearing response which was found in the present study in contrast to the central nervous system stimulating effect of increasing the rearing response due to amphetamine (LAT, 1965; HOLLAND and GUPTA, 1967; GUPTA and GREGORY, 1967).

Another observation made in this study is apparent from Fig. 2a, b, c, namely that up to a certain dose-level, i.e. 8 $\mu\text{g}/\text{kg}$, the drug caused a linear increase in ambulation (stereotyped response) as well as in the exploratory activity of rearing. These doses were such which could be considered normal doses since they were comparable to the usual doses employed for a full behavioural effect in humans. The administration of doses of 32 $\mu\text{g}/\text{kg}$ and doses higher than this revealed interesting results in as much as ambulation (horizontal stereotyped activity) continued to increase with the increased doses, while rearing (vertical stereotyped activity) declined. In other words there was a kind of negative correlation between these two types of stereotyped responses, as against the tendency towards a positive correlation seen with doses

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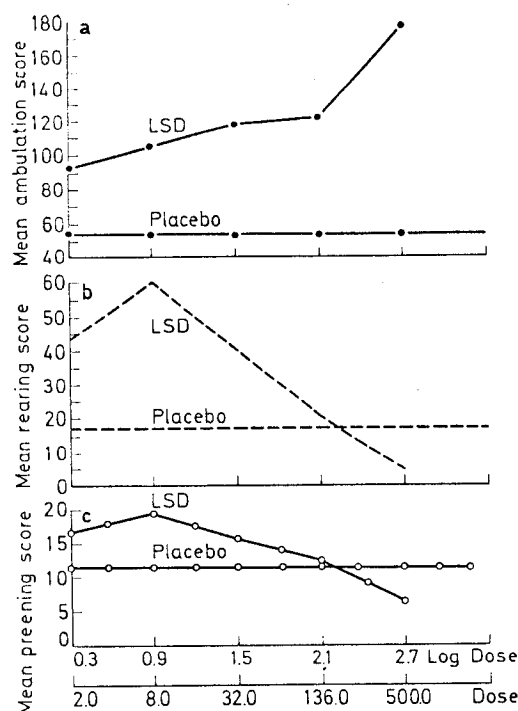


Fig. 2. The responses to varying doses (2, 8, 32, 136 and 500 $\mu\text{g/kg}$) of LSD with reference to placebo. a) Mean ambulation score. b) Mean rearing score. c) Mean preening score in the "Open Field Test" situation

up to 8 $\mu\text{g/kg}$. Decreased vertical stereotyped response in the presence of increased horizontal stereotyped response, the latter being indicative of intact muscular coordination, is positive evidence in favour of the view that vertical stereotypy i.e. rearing activity and its preparatory set (preening) is independent from the horizontal stereotyped activity. On the assumption that the results obtained are specific effects of LSD, it can be suggested that whereas in normal doses LSD increased stereotyped activity with increasing doses, at the higher dose range there was an increase only in that form of stereotyped activity which is simple in performance and for which no serious effort is required on the part of the subject. Thus simple horizontal stereotyped activity increased at the cost of vertical stereotypy and it is, therefore, concluded that overall LSD brought about increase in stereotyped behaviour with increasing doses.

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