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THE EFFECTS OF LYSERGIC ACID DIETHYLAMIDE ON COPULATORY BEHAVIOUR IN THE FEMALE RAT*

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Summary The actions of lysergic acid diethylamide (LSD) on a serotonin- and dopamine-dependent functional test, lordotic behaviour in female rats, and other behaviours were investigated. Increasing doses of LSD inhibited the display of lordosis in increasing numbers of females. Also locomotor activity and habituation of a startle reaction were impaired. Pretreatment with a large single dose of *p*-chlorophenylalanine, which by itself induced lordosis in all subjects tested, caused an enhancement of the LSD effect, prolonging its duration. When *p*-chlorophenylalanine was replaced by α-methyl-*p*-tyrosine, all females showed lordosis by this treatment alone, while a combination with LSD had a significantly briefer effect than this dose of LSD alone. Repeated administration of smaller doses of *p*-chlorophenylalanine did not by itself alter the response level in a group of females, and together with LSD the effect was of a shorter duration than after the single dose of *p*-chlorophenylalanine. Inhibition of lordosis was not related to impairment of locomotor capacity. These differential effects after pretreatment with the synthesis inhibitors in addition to other data discussed indicate that certain functional effects of LSD could be related to increased serotonin activity.

A number of investigators have hypothesized over the years that D-lysergic acid diethylamide (LSD) exerts its behavioural effects by an action on serotonergic neurones. More direct experimental evidence for the relationship between functional effects of LSD and serotonin (5-hydroxytryptamine, 5-HT) was obtained in studies of hindlimb flexion activity of spinalized rat preparations (Andén, Corrodi, Fuxe and Hökfelt, 1968), and recordings of the spontaneous electrical activity of neurones of the midbrain raphé complex (Aghajanian, Foote and Sheard, 1968). Both functions are reported to be dependent on 5-HT and it has been suggested that LSD has a direct 5-HT receptor-stimulating action. There is also recent biochemical evidence suggesting that LSD could be an agonist at dopamine receptor-sites (Creese, Burt and Snyder, 1975).

Lysergic acid diethylamide potently alters a variety of behaviours, most of these with an as yet unclarified relationship to 5-HT. Only in a few cases have these behavioural changes by LSD been related to 5-HT transmission. For example, Appel, Lovell and Freedman (1970) showed that reduction of 5-HT synthesis by *p*-chlorophenylalanine (*p*-CPA) enhanced the LSD-inhibition of bar pressing behaviour, and that this did not occur after a similar reduction of catecholamine synthesis. Components of the copulatory behaviour in the female rat have been demonstrated to be dependent on 5-HT. The frequency of lordotic behaviour in female rats, shown in response to being mounted by the male, has been found to be inhibited after treatments selectively increasing 5-HT neuronal activity (Meyerson, 1964a, b; Meyerson, Eliasson, Lindström, Michanek and Söderlund, 1973). Also dopaminergic activity seems to be involved to some extent, e.g. there is some reduction of lordotic responding after treatment with dihydroxyphenylalanine (Meyerson *et al.*, 1973; Meyerson and Malmnäs, 1977), and the dopamine agonist 1-(2″-pyrimidyl)-4-piperonylpiperazine (ET495) inhibits the behaviour in estrogen-treated rats (Everitt, Fuxe and Hökfelt, 1974). This behaviour is a suitable tool for neuropharmacological investigation, and has the additional advantage of allowing the study of drug effects in intact and conscious animals, thereby avoiding any influence of anaesthesia or surgery that might interfere with or obscure the effects.

The present study employed the lordosis inhibition test for investigation of the effects of LSD under different conditions of monoaminergic activity. The alterations of lordotic behaviour have been compared with the effects of the different treatments on other behaviours with varying degrees of known 5-HT involvement.

MATERIALS AND METHODS

Subjects were female Sprague–Dawley rats weighing 270–330 g. They were kept 5–6/cage in stainless steel cages with tap water and commercial rat chow

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(Anticimex 210) available *ad lib*. The animal room, with forced ventilation, maintained a temperature of 21 ± 1°C and had the light–dark cycle reversed (lights on from 9 p.m. to 9 a.m.).

In a different section of the same room the stud males were housed in large (40 × 40 × 30 cm) individual cages, which also served as test cages. These Wistar males were selected for sexual vigour and trained to a standard level of performance.

Copulatory behaviour (lordosis response)

Female copulatory behaviour is abolished after ovariectomy but can be restored by estrogen followed after a certain time by progesterone treatment (Boling and Blandau, 1939). The females were ovariectomized upon arrival at the laboratory and were rested for two weeks before the first test with hormones was undertaken. This was a standard test to assess the action (frequency of lordosis) of the ordinary hormone treatment in each batch of 10–12 females that constituted a group; members of a group being tested on the same occasion. After another two weeks the hormone treatment was repeated, but on this occasion testing of drug effects was also performed. The animals were normally used in a cross-over experimental design with half the group receiving the compound to be tested, while the other half received saline or other appropriate control injection. Two weeks later these conditions could be reversed for the two subgroups. All testing was performed during the dark period of the animals' light–dark cycle, starting about 4 hr after the beginning of the dark phase.

Copulatory behaviour was induced through injections with estradiol benzoate (10 μg/kg) given at 8 a.m. two days before the actual day of testing. Progesterone, 0.4 mg/animal, was administered 48 hr after estradiol benzoate. This treatment induces lordosis behaviour in about 70% of a group of female rats during the time of peak effect. The response starts appearing about 4 hr after the progesterone injection and reaches a plateau at 5–6 hr.

The effect of LSD was studied on the established behaviour, i.e. about 6 hr after the progesterone injection, when the level of responding normally stays at a plateau for 3–5 hr.

For lordosis testing, each female was brought individually to the cage of the male and observed. A positive response was defined as two consecutive lordoses of a certain quality (with head and perineum clearly raised and tail deviated) in response to mounting by the male. A maximum of six vigorous mounts by no more than two different males was allowed before testing was discontinued for that particular testing occasion and female.

Locomotor activity

The spontaneous motor activity was measured during a 10 min period, when the animal was free to move around and explore in a Macrolon® cage connected to an Animex Activity Meter (Farad Inc., Hägersten, Sweden). The movements of the animal across the electromagnetic field of a tuned oscillator circuit altered the tuning which was recorded automatically and cumulated for a certain period (Svensson and Thieme, 1969). These measurements were obtained under treatment conditions identical with those for the lordosis response, i.e. the hormones and drugs were injected according to an identical schedule. The testing room was lit in one corner away from the testing apparatus by a 25 W bulb.

Vocalization behaviour

Any kind of vocal reaction emitted by the female in response to being touched by the male in the mating situation was recorded. No attempt was made to differentiate intensity or kind of vocalizations nor the tactual stimuli evoking them.

Habituation of the startle reaction to the presentation of repeated sensory stimuli

The response was evoked by rapping a pencil against the side of the table on which the cage containing the animal was placed. The stimuli were presented once every 2 sec and repeated six times. These tests were conducted just before lordosis testing in the same animals.

Statistical tests

Differences between treatments were tested for statistical significance by means of the Chi^2 test (Siegel, 1956) for lordosis behaviour, startle reaction, and vocalization. The locomotor exploration scores were analyzed through the ANOVA test, followed by Newman–Keuls test for comparisons between individual means (Winer, 1971). Statistical analysis with the Chi^2 test was performed between groups of independent subjects. However, in the Tables these groups have been combined into larger groups for certain treatments to make the presentation of results more clear.

Drugs

Estradiol benzoate and progesterone (both from Organon) were dissolved in olive oil and injected subcutaneously. D-Lysergic acid diethylamide tartrate, Sandoz; *p*-chlorophenylalanine methylester HCl, H 69/71, Hässle; α-methyl-*p*-tyrosine methylester HCl (α-MPT) H 44/68, Hässle, were dissolved in saline and injected intraperitoneally in a volume of 1 ml/kg. All drug solutions in saline were freshly made for every testing session.

RESULTS

Lordosis responding

As is evident from Table 1, there was an obvious inhibition of the lordosis response at all doses of LSD tested, as compared with control groups tested with saline. This inhibition became progressively greater with increasing doses. The reduction of the frequency of lordosis reached its maximum 10 min after the

Table 1. Effects of different doses of LSD on the percentage of females showing the lordosis response

Treatment (mg/kg)	Percentage lordosis Time after injection (min) Pretest	10	40	90	180	n
Saline	74	71	79	82	79	38
LSD, 0.10	62	30	58	77	77	86
0.25	68	0	23	73	73	22
0.50	84	0	0	58	90	31

The treatment was given at time 0 min. The pretest was conducted 1 hr before treatment, 5 hr after the progesterone injection (for hormone treatment see Methods).

LSD injection. Signs of recovery of the response started appearing 30 min later at the two lower doses, although the response of a group receiving 0.1 mg/kg LSD was still significantly depressed at this time, as compared to a saline-treated control group ($\chi^2 = 13.31$, d.f. 1; $P < 0.001$). The higher doses gave a longer lasting inhibition and after 0.25 mg/kg LSD the behaviour was significantly more inhibited than after 0.1 mg/kg of the same drug at the 40 min test ($\chi^2 = 7.45$, d.f. 1; $P < 0.01$). The frequency of lordotic responding when mounted by the male in the two groups of females receiving the 0.1 and 0.25 mg/kg doses approached the control level of responding 90 min after drug injection. However, after 0.5 mg/kg LSD the behaviour was still significantly less frequent than after treatment with 0.25 mg/kg at this particular test ($\chi^2 = 5.35$, d.f. 1; $P < 0.05$). Full recovery of the copulatory response of the female subjects was obtained 3 hr after the injection of LSD at all doses.

The serotonin synthesis inhibitor, *p*-CPA (Koe and Weissman, 1966) at a dose of 350 mg/kg given 5 hr before the start of testing brought about a maximal response frequency, which was maintained throughout testing, as is shown in Table 2. In addition, this treatment increased soliciting behaviour such as darting movements in the females and the lordotic posture displayed after this treatment was on the whole more intense than that seen in saline-injected animals.

If LSD was given after pretreatment with *p*-CPA there was a prolongation of the inhibitory effect on lordosis as compared with LSD of an identical dose given alone. This was evident after both the 0.1 and 0.5 mg/kg doses of LSD. At the last test, 3 hr after the LSD injection, full recovery of the response was not obtained after either dose. These differences were statistically significant ($\chi^2 = 13.94$, d.f. 1; $P < 0.001$ and $\chi^2 = 8.39$, d.f. 1; $P < 0.01$) as compared with the 0.1 and the 0.5 mg/kg dose of LSD respectively. The prolonged effect of LSD given after *p*-CPA treatment is even more evident when it is considered that *p*-CPA itself induced a maximal response.

In analogous experiments, *p*-CPA was replaced by the tyrosine hydroxylase inhibitor α-MPT (200 mg/kg). After this compound the level of lordotic responding reached 100% at the 40 min test, i.e. 5 hr plus 40 min after the α-MPT had been injected. In contrast to the prolonged effect of LSD after pretreatment with *p*-CPA recovery from the effect of LSD after α-MPT was already obtained at the 40 min test. Only 10 min after the LSD injection was there any inhibition of lordosis and the magnitude of this effect was significantly smaller than that seen after LSD at 0.1 mg/kg alone ($\chi^2 = 4.20$, d.f. 1; $P < 0.05$). However, this comparison should also consider that the α-MPT treatment gave a higher, however not significantly higher, response relative to saline controls.

Table 2. Effects of LSD on the percentage females showing lordosis response after pretreatment with *p*-chlorophenylalanine (*p*-CPA) and α-methyl-*p*-tyrosine (α-MPT)

Treatment (mg/kg)	Percentage lordosis Time after injection (min) Pretest	10	40	90	180	n
p-CPA, 350	100	100	100	100	100	23
p-CPA, 350 + LSD, 0.1	71	38	25	25	46	24
p-CPA, 350 + LSD, 0.5	90	0	0	20	50	20
α-MPT, 200	88	94	100	100	100	17
α-MPT, 200 + LSD, 0.1	79	58	88	92	96	24

The LSD treatment was given at time 0 min. *p*-CPA and α-MTP were injected 5 hr earlier. For comparison all treatments were tested according to the same schedule. The pretest was conducted 1 hr before time 0 min, 5 hr after the progesterone injection (for hormone treatment see Methods and for saline controls see Table 1).

Table 3. Effects of LSD on the percentage females showing lordosis after pretreatment with repeated doses of *p*-chlorophenylalanine (*p*-CPA)

Treatment (mg/kg)	Percentage lordosis Time after injection (min) Pretest	10	40	90	180	*n*
p-CPA 100 × 3	58	67	67	83	83	12
p-CPA 100 × 3 + LSD, 0.1	71	50	29	75	92	24

The LSD treatment was given at time 0 min. *p*-CPA was injected 24, 48 and 72 hr earlier. For further details see legend to Table 2 and Methods.

Repeated administration of *p*-CPA with testing commenced at the time when 5-HT levels in brain could be expected to be at a very low level (Koe and Weissman, 1966) had no effect on the lordosis response (Table 3). The level of responding remained similar to that obtained in the saline control group (Table 1) throughout testing. Together with 0.1 mg/kg LSD there was a significant lordosis inhibition 40 min after LSD had been injected ($\chi^2 = 6.75$, d.f. 1; $P < 0.01$). At the following tests the response frequency was restored to that of the group treated with *p*-CPA alone. Comparing the effects of LSD after the different *p*-CPA treatments it is found that after repeated *p*-CPA administration, the inhibitory effect of LSD was almost completely over at the 90 min test, while after *p*-CPA (350 mg/kg) the inhibition was still evident at the 180 min test.

Habituation of the startle response

Saline-injected animals rarely responded more than once to the repeated stimulus presentations. The criterion for loss of habituation was therefore decided at three or more consecutive reactions to the stimulus, and the data are presented in terms of habituation or loss of this response. From Table 4 it is evident that there was an increasing loss of habituation with increasing doses of LSD at the 10 min test, as the animals continued to respond. At the 0.25 mg dose statistical significance was reached as tested by the Chi^2 test ($\chi^2 = 7.93$, d.f. 1; $P < 0.01$). Pretreatment with *p*-CPA, which by itself had no inhibitory effect on the habituation reaction as measured in the present study, did not significantly alter the effect of 0.1 mg LSD or 0.5 mg/kg of LSD. Repeated doses of *p*-CPA had a clear effect on habituation. There were significantly more continued startle reactions as compared with saline at the 40 min test ($\chi^2 = 4.04$, d.f. 1; $P < 0.05$). Together with 0.1 mg/kg LSD there was a significantly larger disturbance of the habituation of the startle 10 min after this injection than after repeated *p*-CPA injections alone ($\chi^2 = 4.03$, d.f. 1; $P < 0.05$).

An alteration of the catecholamine synthesis through treatment with α-MPT did not affect the habituation of startles. Neither was there any effect of this compound in combination with 0.1 mg/kg LSD.

Table 4. Effects of LSD alone and after pretreatment with *p*-chlorophenylalanine (*p*-CPA) or α-methyl-*p*-tyrosine (α-MPT) on habituation of the startle reaction

Treatment (mg/kg)	Percentage females that did not habituate Time after injection (min) 10	40	90	*n*
Saline	0	0	0	38
LSD, 0.1	11	0	0	35
0.25	44	10	0	27
0.50	66	11	0	38
p-CPA, 350	0	0	0	12
p-CPA, 350 + LSD, 0.1	0	0	0	23
p-CPA, 350 + LSD, 0.5	55	0	0	20
p-CPA, 100 × 3	25	42	25	12
p-CPA, 100 × 3 + LSD, 0.1	67	50	25	24
α-MPT, 200	0	0	0	12
α-MPT, 200 + LSD, 0.1	0	0	0	12

For testing and injection schedule see legend to Tables 1, 2 and 3.

Table 5. Effects of LSD alone and after pretreatment with *p*-chlorophenylalanine (*p*-CPA) or α-methyl-*p*-tyrosine (α-MPT) on vocalization by the females when touched by the males

Treatment (mg/kg)	Percentage females that vocalized Time after injection (min) 10	40	90	180	*n*
Saline	11	14	3	3	36
LSD, 0.1	39	43	13	4	23
0.25	59	86	9	0	22
0.50	100	100	60	40	16
p-CPA, 350	16	21	21	16	19
p-CPA, 350 + LSD, 0.1	64	50	41	50	22
p-CPA, 350 + LSD, 0.5	30	30	60	60	10
p-CPA, 100 × 3	42	42	25	25	12
p-CPA, 100 × 3 + LSD, 0.1	71	88	42	17	24
α-MPT, 200	6	17	11	22	18
α-MPT, 200 + LSD, 0.1	83	50	10	0	24

For testing and injection schedule see legend to Tables 1, 2 and 3.

Vocalization behaviour

Hormone-treated ovariectomized females rarely vocalize in the mating situation, as is seen from Table 5. However, after LSD-treatment there was a dose-dependent increase of vocalization behaviour of the females when touched in any way by the male. They also responded to being touched by the experimenter. This behaviour was most evident at the 10 and 40 min tests, when the inhibition of the lordosis response was more pronounced. After this time vocalization was practically absent at the 0.1 and 0.25 mg/kg doses of LSD. In a group of females receiving LSD 0.1 mg/kg, vocalization was significantly more frequent than in a comparable group receiving saline at the 10 min test ($\chi^2 = 4.89$, d.f. 1; $P < 0.05$). After the 0.5 mg dose of LSD, vocalization was present in 100% of the experimental females at the first two tests after injection, during which time lordosis was completely inhibited by this particular dose.

p-Chlorophenylalanine at 350 mg/kg, which by itself had no effect on vocalization, prolonged the LSD effect on this behaviour; thus, following the lordosis inhibition very closely. This *p*-CPA treatment still significantly enhanced the LSD effect 180 min after the injection of 0.1 mg/kg ($\chi^2 = 9.76$ d.f. 1; $P < 0.01$). Repeated administration of *p*-CPA had no significant effect, but in combination with LSD there was still significantly more vocalization at the 90 min test than in comparable control group ($\chi^2 = 7.39$ d.f. 1; $p < 0.01$).

Inhibition of catecholamine synthesis by administration of α-MPT also did not change the frequency of vocalization as compared with a saline-injected control group. Together with LSD, however, there was a significant increase of vocalization at the 10 min test beyond that observed after the same dose of LSD by itself ($\chi^2 = 6.55$, d.f. 1; $P < 0.02$). Compared over all conditions tested there is a negative correlation between frequency of lordosis and frequency of vocalization, which is significant ($r_s = -0.67$; $P < 0.05$).

Locomotor activity

Locomotor activity recorded 10 min after the injection of LSD or corresponding control treatment, was affected by all treatments, as can be seen from Table 6. Statistical analysis by means of the analysis of variance test produced a significant effect ($F = 4.00$, d.f. 8/99, $P < 0.01$). Administration of LSD depressed exploratory locomotion increasingly with increasing doses, but only the 0.25 mg/kg dose was significantly different from saline according to the Newman–Keul test. The 0.1 mg/kg dose of LSD and *p*-CPA (100 mg/kg × 3) were the only conditions that did not decrease this behaviour significantly from the saline control condition. These two treatments were also not significantly different from the effect on locomotor exploratory behaviour by the treatments combined.

After *p*-CPA (350 mg/kg) all subjects displayed a clearcut lordosis response but the exploratory locomotor activity was significantly decreased compared with saline treatment. The same effect was obtained when α-MPT was administered. The effects of LSD (0.1 mg/kg) combined with the *p*-CPA or α-MPT treatment were not different from LSD treatment alone, according to the Newman–Keul test.

DISCUSSION

There was a dose-dependent effect by LSD on all behavioural measures in the present study. However, there are differences in sensitivity to the drug between behaviours, and the effects of pretreatments combined with LSD show differences.

Table 6. Mean locomotor activity (number per group = 12)

Treatment (mg/kg)	Score	P compared with saline
Saline	856.3	
LSD, 0.1	612.4	n.s.
0.25	189.3	<0.01
p-CPA, 350	267.3	<0.01
p-CPA, 350 + LSD, 0.1	381.2	<0.01
p-CPA, 100 × 3	763.3	n.s.
p-CPA, 100 × 3 + LSD, 0.1	483.3	<0.01
α-MPT, 200	218.3	<0.01
α-MPT,200 + LSD, 0.1	262.8	<0.01

LSD and saline were given 10 min, p-CPA and α-MPT were given 5 hr before test.
n.s. = not significant.

Lordosis inhibition showed the greatest sensitivity, requiring smaller doses of LSD for a significant effect to appear than did other behaviours. When the drug effects on the habituation disturbance disappeared, lordosis was still significantly inhibited. The differential effect of the two synthesis inhibitors p-CPA and α-MPT together with LSD is in accordance with results obtained by Appel *et al.* (1970) using a bar pressing situation, who similarly observed an enhanced sensitivity to LSD after pretreatment with p-CPA. This was not the case after treatment with α-MPT. The prolonged inhibitory effect of LSD on the lordosis response was only seen when a single high dose of p-CPA was given 5 hr before the LSD treatment. When LSD was injected after pretreatment with repeated p-CPA administration commenced two days before the LSD injection, LSD did not have any effect different from that obtained by the same dose of this drug alone. The functional state of the mechanisms involved in serotonergic transmission is probably different after the one-dose p-CPA regimen and repeated injections of this agent, and the effect of LSD is apparently dependent on this state.

The habituation of the startle reaction was also inhibited by increasing doses of LSD. Increase of startle amplitude and disruption of adaptation to repeated stimulus presentations by LSD have been obtained previously through more refined methods (Key and Bradley, 1960; Davis and Sheard, 1974) and support the present results. Central 5-HT involvement in the elaboration of the startle reaction is suggested from studies using monoamine precursors 5-hydroxytryptophan and dihydroxyphenylalanine (Fechter, 1974). In the present study the habituation was tested in the same subjects as those participating in the tests for lordosis response. It is important to consider that inhibition of the lordosis response means that the behaviour is abolished, whereas the inhibition of the habituation process means that the motor performance, i.e. the startle reaction, continues. This indicates that inhibition of lordosis is specific and not related to impaired motor functions, as doses of LSD which completely inhibited lordosis responding significantly increased the frequency of startle reactions.

No detectable effect was seen on the habituation behaviour by the α-MPT plus LSD treatment compared with these compounds given separately. Repeated p-CPA treatment but not the single dose regimen increased the percentage of females that did not habituate 10 min after the LSD injection. The opposite effect was obtained in the case of p-CPA influence on LSD inhibition of the lordosis response, i.e. the single p-CPA treatment prolonged the LSD effect. Thus, although 5-HT seems to be involved in both behaviours, and there was an inhibition achieved by LSD treatment, there are also differences which could be revealed by changing the dose regimen of p-CPA. It is possible that this difference could be partly due to the fact that gonadal hormones are involved in the activation of lordosis but not necessary for the habituation process.

Vocalization in response to tactile stimuli is apparently not uncommon in rats after different drug treatments (Järbe and Henriksson, 1973). The significant negative correlation between effects on vocalization and lordosis in the present work indicates an interdependence between inhibition of the lordosis and the vocal reaction.

Locomotor activity, as measured in the Animex Activity Meter, can be regarded as the most complex of the behaviours observed. There was a significant impairment by all treatments, with the exception of repeated doses of p-CPA, regardless of their effects on the monoamines. Reduction of locomotion and exploration by LSD in rats has previously been observed, an effect that appears to be dependent on the size and design of the apparatus employed, since the opposite effects also have been obtained (Hughes, 1973). In the present context, information on locomotor activity serves only as a background against which effects on the more specific lordosis response can be evaluated.

The lack of interdependence between locomotor exploratory activity and lordotic behaviour is obvious. The exploratory locomotion was not significantly inhibited or increased, although the lordosis response was significantly inhibited by LSD (0.1 mg/kg) and after *p*-CPA (350 mg/kg) 100% of the females displayed lordosis, while the locomotor activity score was very low and significantly different from the control scores.

When the data on lordosis response, habituation, vocalization and locomotor activity are taken together, it is concluded that the effect of LSD on the lordosis response is specifically related to an action on pathways mediating inhibition of the lordotic behaviour, presumably with a decrease of firing rates in neuronal systems essential for the behaviour, as a consequence.

There is a close correspondence between drug effects on the hindlimb flexion preparation and the lordosis response. Both functions are impaired by monoamine oxidase inhibition (Andén *et al.* 1968; Meyerson, 1964a, b) and monoamine oxidase inhibitors potentiate the effects of 5-hydroxytryptophan. The parallels between these two functions continue, when the effects of LSD are also taken into consideration.

Recently it has been reported that LSD in very low doses exerts a stimulatory effect on lordosis in the female rat (Everitt, Fuxe, Hökfelt and Jonsson, 1975). In that study, however, LSD was employed as a replacement for progesterone and its effects were observed in females treated daily with small amounts of estrogen, which makes the outcome of a direct comparison of the results from these two different testing situations very uncertain. Furthermore, there is evidence that small doses of LSD applied locally by microiontophoresis inhibit firing rates of raphé neurones (Aghajanian, Haigler and Bloom, 1972) presumably by stimulation of presynaptic receptors. Doses more comparable to those that inhibit lordosis responding, on the other hand, also inhibit the postsynaptic firing (Haigler and Aghajanian, 1974). These differences could be involved in different functional effects.

Since increased dopaminergic activity has also been found to decrease the lordosis response, we have to consider that the inhibitory effect of LSD on the lordosis response could be related to serotonergic or dopaminergic activity or both. There is nothing to exclude a dopaminergic action, but the following arguments would favour serotonergic influence as the predominant effect of LSD on lordotic behaviour. In a recent study, in which the effects on the lordosis response of LSD and the dopamine agonist apomorphine were compared, it was demonstrated that the inhibitory effect of apomorphine could be prevented by the dopamine antagonist pimozide, but this was not true for LSD (Eliasson and Meyerson, 1976). In the present study, the results of the differential effects of 5-HT synthesis inhibition compared with catecholamine synthesis inhibition when combined with LSD on the 5-HT dependent lordosis response, further reinforce the opinion that the functional effects of LSD can be mediated by increased 5-HT activity.

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