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LSD-Induced Decrease in Serum Prolactin in Rats (35764)

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Administration of ergot drugs to rats inhibits deciduoma formation (1), pseudopregnancy (2), early pregnancy (2), lactation (3), and mammary tumor growth (4–6). These processes are highly dependent on adequate prolactin release by the pituitary (7). Our laboratory recently demonstrated that ergocornine and ergocryptine markedly reduce serum prolactin levels in rats, both by a direct action on the pituitary and also via the hypothalamus by increasing prolactin inhibiting factor (PIF) activity (8–10). It was of interest therefore, to determine whether D-lysergic acid diethylamide (LSD), a well-known ergot drug, could similarly decrease serum prolactin levels in rats.

Materials and Methods. Female 3- to 4-month-old Sprague-Dawley rats, (Spartan Research Animals, Haslett, Mich.), weighing 200-250 g, were housed in an air-conditioned (74 ± 2°F), light-controlled (lights on from 5 a.m. to 7 p.m.) room. They were fed a standard laboratory diet and provided with water *ad libitum*. At least 2 estrous cycles were followed by taking daily vaginal smears and only 4-day cycling rats were used. On the day of proestrus, a pretreatment blood sample was collected at 11:30 a.m. At 12 noon, the rats were injected ip with 25, 50, or 100 μg of LSD/100 g of body weight in a volume of 0.2 ml of 0.85% NaCl. Control rats were injected with a similar volume of 0.85% NaCl. Blood samples were collected again at 1:30, 3:30, and 5:30 p.m. by cardiac puncture under light ether anesthesia. This method of collecting blood was shown not to alter normal serum prolactin values (11). Serum was separated and stored at −20° until assayed for prolactin by radioimmunoassay (12).

Results. Table I shows that a marked rise occurred in serum prolactin values in control rats on the afternoon of proestrus, in agreement with previous reports (8, 11). By contrast, all doses of LSD injected prevented the normal afternoon rise and evoked a significant decrease in serum prolactin values. The

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TABLE I. Effects of a Single Injection of LSD on Serum Prolactin Levels in Female Rats.[a]

Treatment and no. of rats	Time of proestrous day: Pretreatment 11:30 a.m.	Posttreatment (p.m.) 1:30	3:30	5:30
		(NG/ML)		
Controls (9)	51 ± 5.1	79.4 ± 8.7	126.4 ± 11.0	191.7 ± 8.2
LSD (μg/100 g of body wt)				
25 (9)	54.4 ± 4.9	29.5 ± 3.3	33.9 ± 3.4	37.8 ± 3.8
50 (9)	55.8 ± 4.3	22.9 ± 2.2	30.1 ± 3.3	34.3 ± 3.2
100 (8)	52.5 ± 5.3	17.9 ± 3.4	20.5 ± 3.7	25.2 ± 4.4

[a] Mean ± standard error. All posttreatment serum prolactin values from LSD-treated rats were significantly reduced from pretreatment values ($p < .001$), and were significantly decreased as compared to control values ($p < .0001$).

100-μg dose of LSD produced a significantly greater reduction in serum prolactin concentration than the 25-μg dose ($p<.001$).

Discussion. These results show that LSD, like the other ergot drugs tested by us (8, 9), is a potent inhibitor of prolactin release by the pituitary. All 3 doses of LSD prevented the normal afternoon rise in serum prolactin on the day of proestrus. Earlier we reported that LSD, unlike many other drugs tested, failed to stimulate mammary growth and initiate lactation in virgin female rats (13). On the basis of the present observations, it is probable that LSD inhibits mammary growth and lactation. Whether LSD can influence release of hormones other than prolactin remains to be studied.

Summary. A single ip injection of 25, 50, or 100 μg of LSD (lysergic acid diethylamide)/100 g of body weight into female rats on the morning of proestrus significantly decreased serum prolactin levels, and prevented the normal rise observed in control rats on the afternoon of proestrus. The 100-μg dose of LSD produced a significantly greater decrease in serum prolactin than the 25-μg dose. This action of LSD is shared by other ergot drugs.

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