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Does prolactin control the blood progesterone level on early dioestrus in rats?[1]

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Summary. Bromocriptine treatment on either prooestrus or oestrus in female rats did not affect luteal function on the day of dioestrus 1.

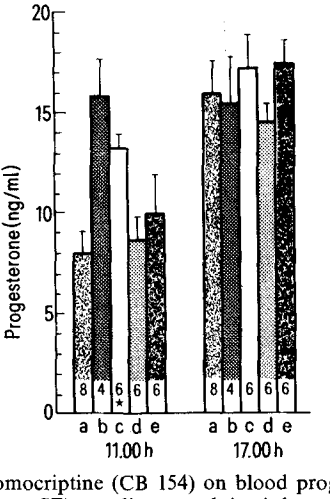
There is some evidence[3] that the corpus luteum can function autonomously during the oustrous cycle in the rat following the preovulatory release of LH on the afternoon of prooestrus. But the role played by the surge of prolactin which also occurs on the afternoon of prooestrus and oestrus remains an unanswered question. Döhler and Wuttke[4] reported that progesterone secretion on the expected day of dioestrus 1 did not differ in prooestrus-mated female rats whose prolactin release had been suppressed by bromocriptine, as compared to nontreated females. However, no data are available at the present time for cyclic animals. The aim of this work was then to determine whether the function of the corpus luteum was dependent on prolactin release during the oestrous cycle in the rat.

Material and methods. Adult virgin 3- to 4-month-old female Wistar rats from our colony, weighing 180–200 g, were used. They were kept under the normal rhythm of natural lighting at a temperature of 22–24 °C. They were fed with a commercial laboratory food and received tap water ad libitum. Oestrous rhythm was monitored by vaginal lavages 6 days a week. Only females which had experienced at least 2 successive 4-day cycles were used. A 4-day sequence consisted of oestrus, dioestrus 1, dioestrus 2 and prooestrus with ovulation taking place during the night following prooestrus[5].

The aim of study 1 was to examine the effects of bromocriptine on progesterone secretion on dioestrus. The females were divided into 5 groups: 1 mg bromocriptine s.c. rendered soluble with tartaric acid was injected on prooestrus, on oestrus and on both prooestrus and oestrus, always at 11.00 h; non-injected animals and tartaric acid injected animals served as controls. All the females were decapitated at the time of the highest activity of the corpus luteum, i.e. on dioestrus 1 at 11.00 h or 17.00 h for the determination of progesterone using a previously described RIA[6].

Blood prolactin values on prooestrus and oestrus in 4-day cyclic female rats injected with bromocriptine (CB 154) at 1100 h on prooestrus and oestrus respectively

Treatment (6 animals per group)	Prolactin (pg/ml) ± SE on prooestrus at 17.00–18.00 h	oestrus at 17.00–18.00 h
CB 154 (1 mg s.c.)	4 ± 2	8 ± 3
Controls	936 ± 283	205 ± 84



Action of bromocriptine (CB 154) on blood progesterone concentration (mean ± SE) on dioestrus 1 in 4-day cyclic female rats: uninjected controls (a); 1 mg tartaric acid at 11.00 h on prooestrus and oestrus (b); 1 mg CB 154 at 11.00 h on prooestrus (c); on oestrus (d); on prooestrus and oestrus (e). * Number of animals in each group.

The progesterone values were expressed in ng/ml. Study 2 was performed to measure blood prolactin concentration at 17.00–18.00 h on prooestrus and oestrus respectively following an injection of 1 mg bromocriptine at 11.00 h on prooestrus and oestrus respectively. Non-injected females served as controls. The prolactin level was determined using the anti-serum S6 and the reference preparation RP1, according to the double antibody radioimmunoassay procedure proposed by the NIAMDD. Radioiodinated ^{125}I-rat prolactin was prepared by New England Nuclear (37 µCi/µg). The intraassay and interassay variation coefficients were 8 and 11% respectively. All serum samples were assayed in triplicate in the same assay. The blood prolactin concentrations were expressed in ng/ml of the RP 1 preparation.

2-way analysis of variance, with orthogonal comparisons, after logarithmic transformation, was used for the statistical analysis of the data.

Results and discussion. As shown in the figure, blood progesterone concentration on dioestrus 1 at 11.00 h did not differ in the 3 groups of females injected with bromocriptine ($F^2_{25} = 2.97$; NS). Taken as a whole, progesterone values in bromocriptine-injected females did not differ from those observed in non-injected controls ($F^1_{25} = 2.05$; NS). Neither did these progesterone values in bromocriptine-injected females differ from those observed in tartaric-acid injected females ($F^1_{25} = 2.66$; NS) although, unexpectedly, a higher progesterone concentration was noted in tartaric-injected females than in non-injected controls ($F^1_{25} = 9.45$; $p < 0.001$). On dioestrus 1 at 17.00 h the blood progesterone concentrations did not differ in the different groups of animals ($F^4_{25} = 0.55$; NS). The table shows that prolactin values were completely depressed for 6 h following bromocriptine injection on eigher prooestrus or oestrus at 11.00 h.

Our observations clearly show that the surges of prolactin which take place on the afternoon of either prooestrus or oestrus are not needed for the function of the corpus luteum during the oestrus cycle in the rat. Bromocriptine treatment, which suppressed both surges, did not alter progesterone secretion at the time of the highest activity of the corpus luteum. These results are in keeping with those of Acker and Alloiteau[3] who showed in hypophysectomized female rats that prolactin was not necessary for luteal activity. For their part Döhler and Wuttke[4] using mated female rats on prooestrus also reported that the corpus luteum could function on the expected day of dioestrus in the absence of any surge of prolactin.

However the question remains as to whether LH is implicated in the control of the corpus luteum activity during the oestrous cycle in the rat. Unpublished results from our laboratory indicate that bromocriptine did not affect LH release on the afternoon of prooestrus. Therefore one may wonder whether the cyclic corpus luteum can actually develop its activity independently of any pituitary control on the day following prooestrus as suggested by in vivo experiments[3,7,8] or in experiments using granulosa cell tissue cultures[9]. Recently, Gallo[10] reported that LH level was higher on dioestrus 1 than on oestrus and dioestrus 2. Therefore the role eventually played by the tonic secretion of LH in the control of the luteal function in the cyclic female rat should be the subject of new investigation.

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Effect of progesterone administration on the number of delayed implantation blastocysts recovered from ovariectomized mice[1]

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Summary. Experimental delay of implantation was induced by ovariectomizing mice on the 4th day after mating. On the 2 days preceding sacrifice, which was on days 7–14 of pregnancy, 3 groups of mice received a s.c. injection of either progesterone (2.0 mg) in oil, oil, or no injection. Progesterone administration significantly reduced the number of blastocysts recovered after flushing excised uteri with culture medium.

Progesterone treatment of ovariectomized mice appears to metabolically alter the delayed implantation blastocysts they contain. Embryos from steroid-treated mothers accumulate ^{14}C-amino acids more slowly than blastocysts from mice not given progesterone[2]. Administration of progesterone also seems to alter the capacity of delayed implantation blastocysts to convert exogenously supplied glucose into CO_2[3]. Moreover, progesterone treatment appears to increase the viability of delayed implantation blastocysts as measured by their ability to grow into normal fetuses upon transfer to surrogate mothers[4]. Alternatively, progesterone might selectively kill or promote the survival of embryos that are metabolically different from those that survive in the absence of progesterone injection, rather than affecting all embryos in a similar manner[2–4]. In the present study we show that the number of diapausing blastocysts obtained by usual techniques is altered by injecting their mothers with progesterone.