

Inhibition by 2-Br- α -Ergocryptine-Mesilate (CB 154) of Suckling-Induced Pituitary Prolactin Depletion in Lactating Rats

In the first communication on the actions of 2-Br- α -ergocryptine-mesilate (CB 154, bromocriptin (DCI)) on prolactin-dependent functions of the rat, two sets of results were compared, i.e. the inhibitory action on implantation of blastocysts and lactation inhibition¹. It was observed that CB 154 is a much weaker inhibitor of lactation in the rat than of implantation. This discrepancy led to the speculation that suckling stimuli might overcome the inhibitory action of CB 154 on prolactin secretion. MENA and GROSVENOR² have reported that in lactating rats which have been separated from their pups for several hours, a depletion of pituitary prolactin occurs when the contact with the young is reestablished. The effect can best be seen on day 14 postpartum. We have used this model to test the above-mentioned speculation.

Material and methods. 70 inseminated female rats were kept in individual cages from day 10 of gestation until the day of the experiment. On day 14 post partum they were assigned to different experimental groups: IA, mother and pups not separated. IB, mother and pups separated for 8 h, then brought together for 30 min. II, same scheme as with IB, but adults injected with 10 mg/kg s.c. CB 154 at a) time of separation (= to); b) to +3h; c) to +6h; d) to +7h; e) to +7½ h; f) to +8 h i.e. immediately before returning the adult to the youngs. Separation of the mothers from their pups was done by putting the adult rats into separate cages at a distance from the young, but in the same room. 30 min after reestablishing the contact between mothers and their pups the adult rats were decapitated. Adults of group IA were decapitated at various times of the experiment. The pituitaries of the killed animals were removed quickly, the adenohypophysis separated, weighed and deepfrozen until used for analysis.

To assess the prolactin content of the anterior pituitaries, the disc-electrophoretic method as used by YANAI and NAGASAWA³ and YOKOYAMA et al.⁴ was applied. As a reference preparation, ovine prolactin of Ferring AB (Malmö) (1000 IU/ampoule) was used. The prolactin bands were measured photodensitometrically (Densitometer TLD 100, Vitatron). Using a standard curve of the reference preparation, readings were converted and expressed as mU per mg anterior pituitary.

Results. The results are collected in the Table. They confirm that renewal of contact for 30 min between lactating rats and their pups after a separation of 8 h on day 14 post-partum produces a marked depletion of prolactin content of the anterior pituitary (groups A vs. B). We have further found that treating the mother rats with 10 mg/kg s.c. at any time during their isolation from the pups prevented this sensory-induced depletion of prolactin (groups B vs. a-f). When comparing the non-separated and CB 154-treated group a-f rats, some fluctuation of prolactin content seems to have occurred: group a) showed significantly lower, group c) significantly higher prolactin content than animals of control group A). These differences cannot be explained from the available data, and it may be questioned whether they are functionally relevant. We wish to stress the fact 10 mg/kg s.c. of CB 154 effectively prevented the sensory-induced depletion of prolactin from the pituitary. Such a dose inhibited lactation by only about 60%¹. Therefore it seems that the weak lactation inhibitory effect of CB 154 can probably not be explained by assuming that the sensory stimulation of the mother rat by her pups will overcome the inhibitory action of CB 154 on prolactin secretion, at least not during day-time.

One might speculate that in rats with established lactation, galactopoiesis is only partially dependent on continuous stimulation by prolactin as e.g. in cattle^{5,6} sheep⁷ and goats⁸, but unlike in dogs⁹, rabbits, pigs or in women¹⁰. Future experiments will then have to analyze the much stronger inhibitory action of some natural ergot alkaloids like ergocornine¹ on lactation in the rat, which activity might be due in part to pharmacological actions unrelated to prolactin secretion, e.g. vasoconstriction.

Résumé. Chez le rat en lactation, après une période d'isolation sensorielle, le renouvellement du contact avec les jeunes produit une chute de la teneur en prolactine de l'hypophyse antérieure. Cette déplétion pituitaire de prolactine peut être supprimée par prétraitements de femelles isolées avec le CB 154 en une dose n'inhibant que partiellement la lactation de ces rats. Les conséquences de ces résultats sont discutées.

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Prolactin content of anterior pituitaries of lactating rats in a MENA-GROSVENOR² experiment

Groups	Mean (mU/mg)	± SD	n
I. controls			
A)	152.2	12.4	13
B)	86.9	10.0	10
II. CB 154 treated			
a)	104.5	14.3	7
b)	153.3	18.8	7
c)	177.4	15.8	5
d)	150.2	22.7	9
e)	131.5	14.0	10
f)	143.7	11.4	10

For explanation of the different groups, see text. Levels of statistical significance of differences between groups: A vs. B = $p < 0.001$; B vs. a-f = $p < 0.01$; A vs. a, c = $p < 0.01$; A vs. b, d-f = n.s.

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