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Influence of exogenous Prolactin on Thyroid uptake of ^{125}I in Rats[1]

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SUMMARY

Prolactin at a daily dose of 500 µg failed to influence thyroidal ^{125}I uptake in sexually mature male and ovariectomized female rats. The lowered mean uptake value in prolactin treated intact females is apparently due to the lack of normal oestrus-associated elevation in iodine accumulation. The possible mechanism by which this could have taken place is discussed.

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INTRODUCTION

Prolactin, an anterior pituitary hormone, is well known for its mammotrophic effects. In lactating rats serum prolactin levels have been shown to be directly related to the suckling stimuli (Amernomori et al, 1970). At the same time serum thyroxine levels were found to be inversely related to the intensity of lactation and supplementation of iodine in the diet could not restore the thyroxine levels back to normal (Lorsheider and Reineke, 1971). The possibility of prolactin being a factor responsible for depressing serum thyroxine levels in rats was investigated by Lorsheider and Reineke (1971), who failed to get any effect. Nevertheless, an inhibitory action for prolactin on thyroid activity has been

suggested in mice (Kwa et al, 1963), rats (Macleod et al, 1966; MacLeod and Abad, 1968) and amphibians (Gona, 1967). In view of these a more detailed study was undertaken to assess the effects of exogenous prolactin on thyroid function in rats and in this report the results of thyroidal ^{125}I uptake are presented.

MATERIALS AND METHODS

Ten to twelve week old albino rats maintained in a light (12 hour photoperiod) and temperature (22 ± 2°C) controlled room were used. They had free access to dietary pellets (Iodine content = 2.5 µg/g) and tap water.

In experiment 1, 18 virgin females and 16 males (caged separately; not more than 4 in one cage) received either Prolactin (500 µg in 0.1 ml 0.9% saline/animal/injection) or Saline (0.1 ml 0.9% saline/animal/injection). The injections were given s.c. once daily for 8 days Vaginal smears of the females were examined every morning between 0900 and 1000 hours.

In experiment 2, 24 virgin females were ovariectomized under ether anaesthesia and allocated to one of the three groups. One week after surgery they were given one of the following treatments (per animal/injection) once daily for 12 days. (1) 500 ug Ovine Prolactin in 0.1 ml 0.9% saline (2) 0.1 ml 0.9% saline (3) 1 mg Progesterone (Sigma) in 0.2 ml Olive oil.

On the last day of treatment all rats were given s.c. 0.1 ml ^{125}I solution (Radiochemicals, Amersham) having a count rate of about 550 counts per second using a precision checked 'repette'. Three samples of the injected solution served as standards. Twelve hours later the animals were killed with an overdose of ether. The thyroid lobes from each rat were carefully dissected out, weighed on a Metler balance and digested in 2 ml 2N NaOH solution at 60°C in a shaker bath. Standards were made up to 2 ml with 2N NaOH solution. A lead shielded well counter connected to a scaler spectrometer (Nuclear Enterprises, Edinburgh) was used for ^{125}I counting. Each sample was counted for 400 seconds. All counts were corrected for back ground activity and ^{125}I uptake as percentage of injected dose was calculated.

Statistical significance was determined using Student's *t* test.

RESULTS

The mean ^{125}I uptake value for prolactin treated normal females was lower ($p < 0.1$) than in the controls (Table 1). On the other hand no discernible change could be noted in the males (Table 2). Since the thyroidal iodine accumulation is known to undergo cyclic changes in females, being highest at oestrus and lowest at dioestrus (Brown-Grant, 1962; Boccabella and Alger, 1967) an attempt was made to distinguish the effect of prolactin from that imposed by cyclic fluctuations. In determining the cyclic stage, vaginal smears on the morning of killing and the day before were taken into consideration. Within the control group, the animals that were in oestrus showed significantly higher ($p < 0.05$) values (11.42 ± 0.40) compared to those in other stages of the cycle (7.16 ± 0.31). In the prolactin treated group, the uptake values obtained for animals in oestrus (8.72 ± 0.83) were not significantly different from those in other stages (7.28 ± 0.28). Thus the values for animals in oestrus in the prolactin treated group was significantly lower ($p < 0.05$) as compared to their counterparts in the control group.

TABLE I

RESPONSES OF SEXUALLY MATURE FEMALE RATS TO PROLACTIN

Treatment	Body weight in g		Organ weights in mg			% ^{125}I uptake by the thyroid
	Initial	Final	Thyroid	Ovary	Uterus	
Prolactin (9)	195.4 ± 3.9	206.1 ± 4.4	10.5 ± 0.9	68.5 ± 2.0	254.0 ± 20.5	7.88 ± 0.61
Saline (9)	199.7 ± 5.2	206.6 ± 5.5	11.1 ± 0.6	74.0 ± 4.3	374.4 ± 56.2	9.73 ± 0.77

Values are expressed as Mean ± S.E.M. Figures in parentheses indicate number of animals.

TABLE II

RESPONSES OF SEXUALLY MATURE MALE RATS TO PROLACTIN

Treatment	Body weight in g		Organ weights in mg			% ^{125}I uptake by the thyroid
	Initial	Final	Thyroid	Testes	Seminal Vesicles	
Prolactin (8)	192.0 ± 9.8	205.3 ± 8.3	11.3 ± 0.5	1181.7 ± 36.5	481.6 ± 23.8	7.54 ± 0.58
Saline (8)	203.4 ± 8.5	224.1 ± 8.6	12.0 ± 0.5	1157.2 ± 41.3	441.0 ± 21.7	7.10 ± 0.43

Values are expressed as Mean ± S.E.M. Figures in parentheses indicate number of animals.

TABLE III

RESPONSES OF OVARIECTOMIZED RATS TO PROLACTIN AND PROGESTERONE

Treatment	Body weight in g		Organ weights in mg		% ^{125}I uptake by the thyroid
	Initial	Final	Thyroid	Uterus	
Prolactin (8)	197.8 ± 7.1	216.5 ± 6.8	13.6 ± 0.9	111.2 ± 15.5	6.61 ± 0.43
Progesterone (7)	187.2 ± 8.7	206.1 ± 9.2	14.2 ± 0.5	106.1 ± 7.5	7.27 ± 0.41
Saline (8)	191.6 ± 8.9	215.5 ± 8.7	13.1 ± 0.4	101.7 ± 3.5	7.02 ± 0.30

Values are expressed as Mean ± S.E.M. Figures in parentheses indicate number of animals.

Study of the vaginal smears showed that 2 females in the group receiving prolactin remained in persistent dioestrus while in others the appearance of vaginal cornification was delayed by 1-2 days. Uterine ballooning of proestrus (Schwartz, 1969) was noted in 3 control females. None of the progesterone treated animals showed this, resulting in lowered uterine weights ($p < 0.1$) compared to the control group.

In ovariectomized rats the iodine accumulation was significantly lower ($p < 0.01$) than in normal females. Neither Prolactin nor Progesterone treatment showed any effect on ^{125}I uptake values in ovariectomized rats.

DISCUSSION

The results of this investigation failed to show a direct effect for prolactin on thyroid function as measured by ^{125}I accumulation. The lowered mean uptake value in prolactin treated normal females does not appear to be the result of a general depression in all the animals, but due to the lack of elevation in iodine accumulation that normally takes place during oestrus. This could be an indirect effect mediated via the ovary. Available evidence indicates that prolactin is luteotrophic in rats (Rothchild, 1966). Since exogenous progesterone failed to elevate the uptake values in ovariectomized females, an increased progesterone secretion in prolactin treated normal females could not have been by itself responsible for the changes observed in the present investigation. However, a role for progesterone in the presence of oestrogens cannot be ruled out.

Oestrogen treatment in ovariectomized rats has been reported to raise thyroidal ^{131}I uptake (Brown-Grant, 1962). If so, the cyclic rise in iodine accumulation during oestrus could be the result of a rise in oestrogen levels that occurs in rats at a critical period in late dioestrus and is necessary to stimulate the release of ovulating hormone and ovulation (Hagino and Goldzieher, 1970). Delay in the recurrence of oestrus, lack of uterine ballooning of proestrus and reduced uterine weights in the prolactin treated group indicate the possibility of prolactin having interferred in oestrogen production. According to this rationale, prolactin might have lowered oestrogen levels during the critical time in late dioestrus and thereby disturbed the oestrus associated elevation of thyroidal iodine accumulation.

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