Pharmacology Biochemistry & Behavior, Vol. 32, pp. 157–162. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/89 $3.00 + .00

Possible Prolactin-Mediated Effects of Melatonin on Gonadotropin Secretion in the Rat

A. I. ESQUIFINO,*[1] M. A. VILLANÚA, C. AGRASAL* AND J. A. F. TRESGUERRES

*Departamentos de *Bioquimíca y Fisiología, Facultad de Medicina Universidad Complutense, Madrid, Spain*

Received 29 March 1988

ESQUIFINO, A. I., M. A. VILLANÚA, C. AGRASAL AND J. A. F. TRESGUERRES. *Possible prolactin-mediated effects of melatonin on gonadotropin secretion in the rat.* PHARMACOL BIOCHEM BEHAV 32(1) 157–162, 1989.— Melatonin administration to pituitary-grafted male and female rats resulted in a marked decrease of previously high plasma prolactin levels, while an increase in prolactin levels was observed in sham-operated controls. The latter effect was significant only in males. Treatment with melatonin did not modify basal LH hormone levels or LH responses to luteinizing hormone-releasing hormone (LHRH) in sham-operated rats of either sex. However, in pituitary-grafted females, melatonin increased both basal and LHRH-stimulated LH levels towards values recorded in sham-operated controls. No effects on basal LH levels were detected in grafted males under melatonin treatment, but the response of LH to LHRH was markedly increased and no longer differed from the values measured in sham-operated control animals pretreated with saline. Melatonin did not affect follicle stimulating hormone (FSH) levels except for an increase in FSH response to LHRH in grafted females. These findings suggest the existence of sex-dependent effects of melatonin on LH and FSH secretions. These effects of melatonin may be mediated by the different plasma prolactin levels in pituitary-grafted and sham-operated rats.

Prolactin Melatonin LH FSH Gonadotropins

PROLACTIN and gonadotropin secretion are controlled by mechanisms which appear to be closely related (2, 7, 19, 26). Thus, an inverse relationship exists between prolactin and LH levels in a number of physiological, pathophysiological and experimental situations (15, 16, 35).

It is well established that melatonin can inhibit gonadotropin release (36). Since melatonin can also modulate prolactin secretion and, conversely, prolactin can affect the pineal gland via specific receptors (11, 13, 17, 20), we were interested in the possibility that melatonin and prolactin may interact to exert modulatory effects on the reproductive axis.

The aim of the present investigation was to examine the interactive effects of melatonin and chronic hyperprolactinemia on the regulation of LH and FSH release in male and female rats.

METHOD

General Conditions and Sampling

Male and female rats of the Wistar strain were kept under controlled conditions of lighting (12 hr light:12 hr darkness; lights on from 08:00 hr) and temperature (22±2°C). They were fed ad lib with Sanders rat chow (Madrid, Spain).

Heparinized blood samples were taken from the external jugular vein under very light ether anesthesia. The samples were immediately centrifuged at 4°C (1500×g) for 15 minutes and the plasma was kept frozen until analyzed.

Induction of Hyperprolactinemia

One pituitary gland (pars distalis) from female litter-mate donors was transplanted under the right kidney capsule of male and female recipients at the age of 30 days (47). Rats of the same age were sham operated and served as controls. Vaginal smears were taken for at least 20 days before melatonin administration and only animals showing diestrous smears were used in this study for both beginning of treatment and day of sampling.

Melatonin Administration

Starting two months after pituitary transplantation or sham surgery, half of the animals from each group were treated with 200 μg of melatonin per day. Melatonin was dissolved in a mixture of saline and ethanol (1%) and injected IP. The remaining animals received injections of vehicle alone. The treatments were given daily for 7 days and always

[1]Requests for reprints should be addressed to A. I. Esquifino, Ph.D., Dpto. de Bioquímica, Facultad de Medicina, Universidad Complutense, 28040 Madrid, Spain.

TABLE 1

PLASMA PROLACTIN, LH AND FSH LEVELS IN FEMALE RATS

		Day 0	Day 1	Day 2	Day 3	Day 5	Day 7
Prolactin	C.S.	21 ± 3	23 ± 2	21 ± 2	21 ± 3	24 ± 2	21 ± 3
(μg/l)	E.S.	143 ± 13‡	209 ± 20‡	157 ± 13‡	151 ± 12‡	186 ± 18‡	131 ± 16‡
	C.M.	21 ± 3	29 ± 4	26 ± 5	33 ± 5	37 ± 7	33 ± 9
	E.M.	143 ± 13	38 ± 7#	29 ± 4#	27 ± 3#	28 ± 4#	24 ± 3#
LH	C.S.	35 ± 1	39 ± 4	35 ± 4	31 ± 1	38 ± 3	38 ± 5
(μg/l)	E.S.	19 ± 2‡	22 ± 2†	24 ± 2*	17 ± 2‡	21 ± 3†	22 ± 2*
	C.M.	35 ± 1	39 ± 5	32 ± 4	28 ± 3	28 ± 4	33 ± 3
	E.M.	19 ± 2	42 ± 7§	36 ± 4§	29 ± 5	29 ± 3	28 ± 4
FSH	C.S.	197 ± 28	207 ± 27	178 ± 21	190 ± 21	211 ± 19	172 ± 20
(μg/l)	E.S.	310 ± 55	172 ± 13	328 ± 77	255 ± 87	231 ± 51	175 ± 46
	C.M.	197 ± 28	153 ± 13	278 ± 47	255 ± 62	401 ± 67	224 ± 37
	E.M.	310 ± 55	220 ± 44	239 ± 36	187 ± 15	175 ± 10	179 ± 21

Effects of chronic treatment with melatonin (M, 200 μg/rat per day, for 7 days IP) or saline (S) in control (CM or CS) and grafted female rats (EM or ES) on plasma concentrations of prolactin, LH and FSH. Values are expressed as mean ± S.E.M. (n=10 animals in each group). Statistical analysis was performed through a "paired comparison of means" test.

*$p<0.05$, †$p<0.01$, ‡$p<0.001$ vs. CS group.

§$p<0.05$, ¶$p<0.01$, #$p<0.001$ vs. ES group.

5 hours prior to the onset of the dark period as described by Tamarkin *et al.* (42).

Hormonal Determinations

Plasma levels of prolactin, LH and FSH were measured by specific double-antibody radioimmunoassay systems using materials kindly supplied by NIH (Bethesda, MD) and previously validated in our laboratory (46). The results were expressed in μg/l in terms of the respective RP-1 reference preparations.

To avoid the interassay variability, all of the samples were measured in the same assay as in our previous studies (44). Basal hormonal levels were determined at 10 a.m. before and on days 1, 2, 3, 5 and 7 of the melatonin treatment.

Luteinizing Hormone-Releasing Hormone Test

A stimulatory test was performed on day 7 of treatment by the IP administration of 1 μg of synthetic LHRH (Lufo-ran, Serono, Madrid, Spain) to all rats. Blood samples were obtained immediately before (10:00 a.m.) and 30 minutes after LHRH injection, according to previous data from our laboratory (44).

Statistics

Statistical analysis was performed by means of "a paired comparison of mean" method (14,43), which tests for the homogenity of variance between groups and, depending on the result, utilizes either F or *t* statistic for individual comparisons.

RESULTS

There was a marked increase in plasma prolactin levels (Table 1) in pituitary-grafted female rats 60 days after the transplant operation (day 0) as compared to the sham-operated group (Table 1, $p<0.001$). Melatonin treatment resulted in a marked decrease in the previously elevated prolactin levels in grafted female rats as compared to saline-treated grafted rats in which elevated plasma prolactin levels were maintained throughout the study period. In sham-operated rats, melatonin treatment did not affect plasma prolactin levels. Plasma LH levels were significantly suppressed in grafted rats 60 days after the transplant operation (day 0) (Table 1) as compared to sham-operated controls ($p<0.001$). Melatonin did not affect plasma LH levels in the sham-operated rats but induced a rise in plasma LH levels in the grafted animals returning concentrations to those seen in the saline-injected sham-operated controls.

There were no differences in basal plasma FSH levels between grafted and control rats (day 0, Table 1). During melatonin treatment there was a slight increase in FSH levels in control animals, and a slight decrease in grafted animals. Similar patterns of the evolution of FSH levels were observed in both control and grafted rats treated with the vehicle. Melatonin administration increased plasma FSH levels only in control rats on day 5 of treatment ($p<0.05$).

Both basal and LHRH-stimulated LH levels were significantly lower in saline-injected grafted female rats than in the corresponding sham-operated controls (Fig. 1, $p<0.05$ and $p<0.01$, respectively). Administration of melatonin to grafted rats increased basal LH values to those observed in saline-treated sham-operated rats. No effects were observed in sham-operated rats. However, melatonin treatment greatly augmented the LH response to LHRH stimulation in grafted rats as compared to the response measured in saline-treated grafted animals ($p<0.001$). Plasma LH response to LHRH in sham-operated control rats was not modified by melatonin treatment.

Basal FSH levels were similar in all groups studied (Fig. 1) regardless of treatment. Plasma FSH responses to LHRH were similar in saline-treated grafted and control animals and

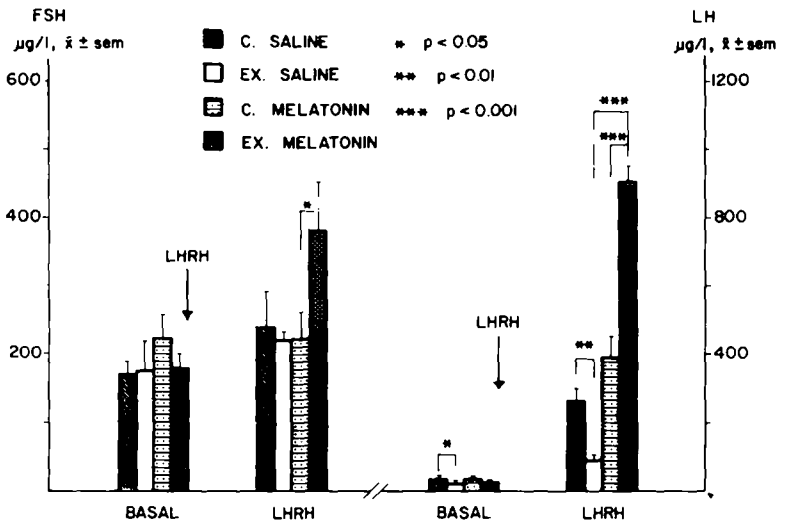

FIG. 1. Plasma concentrations of LH and FSH 30 min after a LH-releasing hormone (LHRH) challenge (1 μg IP) on day 7 of saline (S) or melatonin (M) (200 μg/rat/day) administration in pituitary-grafted (ES,EM) or sham-operated (CS,CM) female rats. Values are expressed as mean±S.E.M. (n=10 animals in each group). Statistical analysis was performed through a "paired comparison of means" test. *$p<0.05$, **$p<0.01$, ***$p<0.001$.

TABLE 2

PLASMA PROLACTIN, LH AND FSH LEVELS IN MALE RATS

		Day 0	Day 1	Day 2	Day 3	Day 5	Day 7
Prolactin	C.S.	23 ± 2	21 ± 3	25 ± 2	22 ± 1	18 ± 2	26 ± 2
(μg/l)	E.S.	152 ± 18‡	119 ± 11‡	122 ± 7‡	115 ± 7‡	122 ± 15‡	165 ± 20‡
	C.M.	23 ± 2	72 ± 20	65 ± 14	110 ± 19	105 ± 17	115 ± 21
	E.M.	152 ± 18	20 ± 2#	17 ± 2#	17 ± 1#	18 ± 1#	19 ± 2#
LH	C.S.	35 ± 4	41 ± 2	37 ± 3	35 ± 2	36 ± 4	40 ± 3
(μg/l)	E.S.	14 ± 2‡	25 ± 3‡	19 ± 3‡	17 ± 2‡	18 ± 3‡	20 ± 2‡
	C.M.	35 ± 4	33 ± 5	44 ± 2	41 ± 4	47 ± 4	47 ± 2
	E.M.	14 ± 2	23 ± 3	24 ± 3	13 ± 2	18 ± 3	22 ± 2
FSH	C.S.	339 ± 44	402 ± 30	556 ± 60	274 ± 36	340 ± 60	374 ± 7
(μg/l)	E.S.	246 ± 56	338 ± 35	416 ± 65	252 ± 28	377 ± 61	455 ± 36
	C.M.	339 ± 44	522 ± 54	503 ± 43	519 ± 63†	497 ± 60	480 ± 51
	E.M.	246 ± 56	380 ± 27	352 ± 26	350 ± 15¶	369 ± 55	337 ± 57

Effects of chronic treatment with melatonin (M, 200 μg/rat per day, for 7 days IP) or saline (S) in control (CM or CS) and grafted male rats (EM or ES) on plasma concentrations of prolactin, LH and FSH. Values are expressed as mean ± S.E.M. (n=10 animals in each group). Statistical analysis was performed through a "paired comparison of means" test.

*$p<0.05$, †$p<0.01$, ‡$p<0.001$ vs. CS group.

§$p<0.05$, ¶$p<0.01$, #$p<0.001$ vs. ES group.

in sham-operated melatonin-treated females. However, a marked increase in the FSH response to LHRH was seen in the grafted rats after melatonin treatment ($p<0.05$ compared to any other group).

In pituitary-grafted male rats, plasma prolactin levels were markedly increased 60 days after the transplant operation (day 0) (Table 2) as compared to sham-operated controls ($p<0.001$). Melatonin treatment markedly reduced the previously elevated plasma prolactin levels in grafted animals and increased plasma prolactin in sham-operated controls. These changes were maintained during the whole period of treatment.

Plasma LH levels were suppressed in grafted male rats as compared to sham-operated controls (day 0, $p<0.001$) and did not change during the period of saline or melatonin treatment (Table 2).

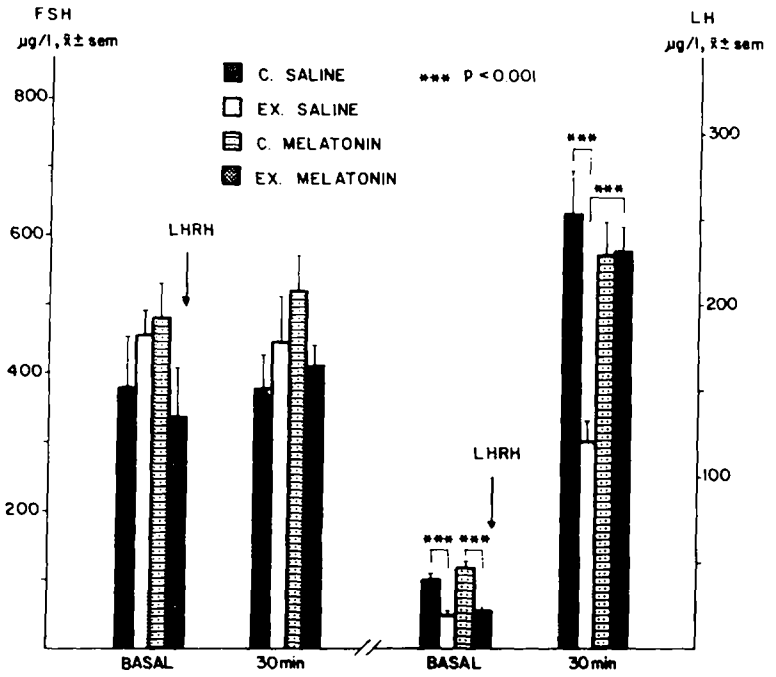

FIG. 2. Plasma concentrations of LH and FSH 30 min after a LH-releasing hormone (LHRH) challenge (1 μg IP) on day 7 of saline (S) or melatonin (M) (200 μg/rat/day) administration in pituitary-grafted (ES.EM) or sham-operated (CS.CM) male rats. Values are expressed as mean ± S.E.M. (n = 10 animals in each group). Statistical analysis was performed through a "paired comparison of means" test. $*p<0.05$, $**p<0.001$.

Plasma FSH levels measured on day 0 did not differ between sham-operated and grafted male rats. There was a significant increase in FSH levels on day 3 of melatonin treatment in both control and grafted animals. No differences in the concentration of FSH were observed at any other time point examined (Table 2).

Pituitary transplants reduced both basal and LHRH-stimulated plasma LH levels in male rats (Fig. 2, $p<0.001$). Melatonin did not overcome the reduction in basal LH levels, but normalized the LH response to LHRH stimulation. In contrast to the results obtained in the females, LH levels measured in melatonin-treated grafted males 30 min after LHRH injection were similar to, rather than greater than the corresponding values measured in grafted animals pretreated with saline.

None of the treatments affected basal or LHRH-stimulated plasma FSH levels in male rats.

DISCUSSION

In the present study, blood samples were drawn from the external jugular vein immediately after induction of very light ether anesthesia. We have previously demonstrated that hormone levels measured in samples collected in this manner do not differ from the values measured in blood collected by decapitation (44). Also, other authors have not found any differences using similar protocols (12, 37, 38, 48).

Transplantation of one anterior pituitary gland under the renal capsule at 30 days of age induced a significant increase in peripheral plasma prolactin levels in the recipient animal as was expected from earlier observations in this and other laboratories (3, 16, 44). We have previously demonstrated that the increase in plasma prolactin levels in pituitary-grafted animals is associated with a significant decrease in the prolactin content of the in situ pituitary (45), suggesting that most of the prolactin present in the circulation originates from the ectopic pituitary tissue.

Prolactin values measured in pituitary-grafted rats in the present study were similar to those observed earlier by our group using the same protocol (16, 44, 45) and higher than those usually reported in animals grafted after puberty (3, 4, 47). This suggests that prepubertal pituitary transplantation is more effective in increasing plasma prolactin levels.

The effects of ectopic pituitary transplants on plasma LH and FSH levels confirm previous findings from this group (15, 16, 44–47) and from other laboratories (2–4, 19, 37), and are consistent with the inhibitory influence of hyperprolactinemia on gonadotropin release. The main source of plasma LH and FSH in grafted rats seems to be in situ pituitary, because the release of gonadotropins from the ectopic gland is minimal and approaches the limit of detectability (25).

Melatonin treatment was followed by a marked decrease in plasma prolactin levels in grafted animals of both sexes. In contrast, identical treatment significantly increased plasma prolactin levels in sham-operated males and appeared to increase them also in sham-operated females. To our knowledge, this is the first study of melatonin effects in pituitary-grafted animals. Since the ectopic pituitary is the main source of prolactin in these animals, the possibility of a direct action of exogenous melatonin at the ectopic pituitary

tissue has to be suspected. However, there is evidence that the hypothalamic catecholaminergic neurons are the most likely site of action of exogenous melatonin (1,41).

Increased plasma prolactin levels in melatonin-treated sham-operated rats in the present study are consistent with some previous reports (5, 24, 39). However, other workers reported no modifications in plasma PRL levels after melatonin treatment (6). These discrepancies could be due to the use of different experimental models such as blinded anosmic (5, 6, 28) or pinealectomized rats (28), and different doses of melatonin (8,21). The discrepancies could be also related to a different sensitivity of the hypothalamic pituitary axis to exogenous melatonin in the rat as compared to other species (32).

Basal plasma LH levels were suppressed in saline-treated grafted female rats and showed a significant recovery after melatonin treatment. This melatonin-induced increase in plasma LH was associated with the reduction in plasma prolactin levels. No changes in gonadotrophin levels were detected during melatonin treatment in sham-operated rats. Other authors reported a reduction in plasma LH levels after melatonin treatment in intact rats (31,33). This unexpected difference between the response of intact and sham-operated rats to melatonin might be due to differences in strain, age or dose of melatonin used. In addition, the time of melatonin administration during the light/dark cycle may be critical (22).

The effects of melatonin on plasma prolactin and LH levels in the present study could have been due to its action(s) at the hypothalamic level (2, 34, 41) and may have involved counteracting the effects of hyperprolactinemia on the hypothalamus (10, 18, 29, 30, 40). In addition, melatonin may have affected gonadotropin secretion at the pituitary level by counteracting the desensitizing effect of hyperprolactinemia on pituitary response to LHRH (44). The latter mechanism of melatonin action is supported by the increased response of FSH to LHRH in grafted rats after melatonin treatment.

In pituitary-grafted males, the reduction of prolactin levels during melatonin treatment was not followed by restoration of plasma gonadotropin levels. This might suggest that the hypothalamic pituitary-gonadal axis is less sensitive to pineal influences in the male than in the female (21). Partial recovery of FSH levels was detected only on day 3 of melatonin treatment of pituitary-grafted males. Thus, it would appear that this pineal indol was able to change only the sensitivity of the pituitary to external stimuli, counteracting the effects of hyperprolactinemia on LH response to LHRH challenge (23). Melatonin did not seem to modify the FSH response to LHRH. If melatonin is exerting its modulatory effects at both the hypothalamic and the pituitary level, as has been shown previously (1, 34, 41, 44), our data suggest that the former effect is less evident in males (21) and only the latter may be operational in immature rats (27).

The existence of pronounced differences between male and female rats in the response of their plasma hormone levels to exogenous melatonin suggests that sexual hormone milieu influences melatonin effects. The possibility of a peripheral action of melatonin at the gonadal level should be also taken into account in view of a recent report of suppressive effects of melatonin on ovarian steroidogenesis (9).

The present study shows differential effects of melatonin on plasma prolactin and gonadotropin levels in pituitary-grafted as compared to sham-operated control rats. Melatonin appears to counteract the effects of hyperprolactinemia on the hypothalamic pituitary-ovarian-axis in female rats by acting at both the hypothalamic and the pituitary level. In male rats, melatonin was not able to counteract the effects of hyperprolactinemia on the hypothalamic-pituitary-testicular axis, suggesting a sex dependent mechanism of action. Moreover, our results suggest that prevailing plasma prolactin levels can profoundly influence the effects of melatonin on adenohypophyseal hormone release.

ACKNOWLEDGEMENTS

This work was made possible by Grant No. 83/108 from the Spanish-USA Joint Committee (for Scientifical and Technological Cooperation). The critical review of the manuscript by Prof. A. Bartke is gratefully acknowledged. We are indebted to the National Hormone and Pituitary Program for the gift of the reagents for prolactin, LH and FSH measurements, and to Mrs. Kraus and Calvo for technical assistance.

REFERENCES

1. Anton-Tay, F. Melatonin: Effects on brain function. Adv. Biochem. Psychopharmacol. 11:315–324; 1974.
2. Bartke, A. Role of prolactin in reproduction in male mammals. Fed. Proc. 39:2577–2581; 1980.
3. Bartke, A.; Smith, M. S.; Michael, S. D.; Peron, F. G.; Dalterio, S. Effects of experimentally-induced chronic hyperprolactinemia on testosterone and gonadotropin levels in male rats and mice. Endocrinology 100:182–186; 1977.
4. Bartke, A.; Goldman, B. D.; Bex, F. J.; Kelch, R. P.; Smith, M. S.; Dalterio, S.; Doherty, P. C. Effects of prolactin on testicular regression and recrudescence in the Golden hamster. Endocrinology 106:167–172; 1980.
5. Blask, D. E.; Reiter, R. J. The pineal gland of the blind-anosmic female rat: its influence on medial basal hypothalamic LRH, PIF and/or PRF activity in vivo. Neuroendocrinology 17:362–366; 1975.
6. Blask, D. E.; Reiter, R. J. Pituitary and plasma LH and prolactin levels in female rats rendered blind and anosmic: Influence on the pineal gland. Biol. Reprod. 12:329–332; 1975.
7. Bohnet, H. G.; Schneider, H. P. G. Prolactin as cause of anovulation. In: Crosignani, P. G.; Robyn, C. C., eds. Prolactin and human reproduction. London: Academic Press; 1977:153–159.
8. Brown, G. M.; Seggie, J.; Grota, L. J. Serum melatonin response to melatonin administration in the Syrian hamster. Neuroendocrinology 41:31–35; 1985.
9. Brzezinski, A.; Seibel, M. M.; Lynch, H. J.; Deng, M. H.; Wurtman, R. J. Melatonin in human preovulatory follicular fluid. J. Clin. Endocrinol. Metab. 64:865–867; 1987.
10. Bybee, D. E.; Nakawatase, C.; Szabo, M.; Frohman, L. A. Inhibitory feedback effects of PRL on its secretion involve CNS dopaminergic mediation. Neuroendocrinology 36:27–32; 1983.
11. Cardinali, D. P. Molecular mechanisms of neuroendocrine integration in the central nervous system: An approach through the study of the pineal gland and its innervating sympathetic pathway. Psychoneuroendocrinology 8:3–30; 1983.
12. Cardinali, D. P.; Boado, R. J.; Vacas, M. I.; Deza, S. Changes in growth hormone and prolactin release after superior cervical ganglionectomy of rats. Brain Res. 363:350–353; 1986.

13. Cardinali, D. P.; Vacas, M. I.; Keller Sarmiento, M. I.; Etchegoyen, G. S.; Pereyra, E. N.; Chuluyan, H. E. Neuroendocrine integrative mechanisms in mammalian pineal gland: Effects of steroid and adenohypophysial hormones on melatonin synthesis in vitro. J. Steroid. Biochem. 27:565–572; 1987.
14. Diem, K.; Lentner, C. Tablas científicas. Barcelona: Documenta Geigy, Division Farmacia; 1975.
15. Esquifino, A. I. Estudio de un modelo de hiperproalctinemia experimental. Tesis Doctoral. Universidad Autónoma, Madrid, 1979.
16. Esquifino, A. I.; Ramos, J. A.; Tresguerres, J. A. F. Possible role of dopamine in changes in LH and prolactin concentrations after experimentally induced hyperprolactinemia in rats. J. Endocrinol. 100:141–148; 1984.
17. Esquifino, A. I.; Villanúa, M. A.; Agrasal, C.; Tresguerres, J. A. F. Interrelationships in the regulatory mechanisms of melatonin and prolactin secretions. In: The proceedings of the workshop on the pineal gland. Salamanca; 1986:28–31.
18. Esquifino, A. I.; Fernández, J. F.; Bartke, A.; Agrasal, C.; Steger, R.; Cebeira, M. Prolactin increases norepinephrine and dopamine turnover in the median-eminence of hypophysectomized female rats. Neuroendocrinol. Lett. 9:5–14; 1987.
19. Judd, S. J.; Rakoff, J. S.; Yen, S. S. C. Inhibition of gonadotropin and PRL release by DA: Effect of endogenous estradiol levels. J. Clin. Endocrinol. Metab. 47:494–498; 1978.
20. Karasek, M.; Lewinsky, A.; Hansen, J. T.; Reiter, R. J. Influence of hypophysectomy and prolactin in the rat pinealocyte: a quantitative ultrastructural study. Reprod. Nutr. Dev. 22:785–787; 1982.
21. Lang, U.; Auber, M. L.; Conne, B. S.; Bradtke, J. C.; Sizonenko, P. C. Influence of exogenous melatonin and melatonin secretion and the neuroendocrine reproductive axis of intact male rats during sexual maturation. Endocrinology 112:1578–1584; 1983.
22. Lang, U.; Rivest, R. W.; Schlaepfer, L. V.; Bradtke, J. C.; Aubert, M. L.; Sizonenko, P. C. Diurnal rhythm of melatonin action on sexual maturation of males rats. Neuroendocrinology 38:261–268; 1984.
23. Lewis, C. E.; Fink, G.; Dow, R. C.; Morris, J. F. Hyperprolactinemia induced by pituitary isografts suppresses the priming effect of LH-releasing hormone in normal and hypogonadal mice. Neuroendocrinology 43:584–589; 1986.
24. Lu, K.; Meites, J. Effects of serotonin precursors and melatonin on serum prolactin release in rats. Endocrinology 93:152–155; 1973.
25. Lu, K. H.; Grandison, L.; Huang, H. H.; Marshall, S.; Meites, J. Relation of gonadotropin secretion by pituitary grafts to spermatogenesis in hypophysectomized male rats. Endocrinology 100:380–386; 1977.
26. McNeilly, A. J.; Sharpe, R. M.; Davidson, D. W.; Fraser, H. M. Inhibition of gonadotrophin secretion by induced hyperprolactinemia in the male rat. J. Endocrinol. 79:59–68; 1978.
27. Martin, J. E.; Sattler, C. Selectivity of melatonin pituitary inhibition for luteinizing hormone-releasing hormone. Neuroendocrinology 34:112–116; 1982.
28. Moore, K. E.; Demarest, K. T.; Johnston, C. A. Influence of PRL on dopaminergic neuronal systems in the hypothalamus. Fed. Proc. 39:2912–2916; 1980.
29. Morgan, W. W.; Herbert, D. C. Early responses of the dopaminergic tubero-infundibular neurons to anterior pituitary homografts. Neuroendocrinology 31:215–221; 1980.
30. Morgan, W. W.; Herbert, D. C.; Pfeil, K. A. The effect of hypophysectomy and subsequent prolactin replacement or of elevated prolactin alone on median eminence noradrenaline and dopamine in the rat. Endocrinology 100:1584–1591; 1982.
31. Motta, M.; Fraschini, F.; Martini, L. Endocrine effects of pineal gland and of melatonin. Proc. Soc. Exp. Biol. Med. 126:431–435; 1967.
32. Nelson, R. J.; Bamat, M. K.; Zucker, I. Photoperiodic regulation of testis function in rats: Mediation by a circadian mechanism. Biol. Reprod. 26:329–335; 1982.
33. Nordlund, J.; Lerner, A. B. The effects of oral melatonin on skin color and on the release of pituitary hormones. J. Clin. Endocrinol. Metab. 45:768–774; 1977.
34. Quay, W. B. General biochemistry of the pineal gland of mammals. In: The pineal gland. Boca Raton, FL: C.R.C. Press; 1981:173–198.
35. Quigley, M. E.; Judd, S. J.; Gilliland, G. B.; Yen, S. S. C. Effects of dopamine antagonist on the release of gonadotrophin and prolactin in normal women with hyperprolactinemic anovulation. J. Clin. Endocrinol. Metab. 48:718–721; 1979.
36. Reiter, R. J. Neuroendocrinology effects of the pineal gland and of melatonin. In: Ganong, W. F.; Martini, L., eds. Frontiers in neuroendocrinology. New York: Academic Press; 1982:287–316.
37. Riegle, G. D.; Meites, J. Effects of aging on LH and PRL after LHRH, L-dopa, methyldopa and stress in male rats. Proc. Soc. Exp. Biol. Med. 151:507–511; 1976.
38. Sellers, K. J.; Smith, M. S.; Rojas, F. J.; Asch, R. H.; Schally, A. V.; Bartke, A. Effects of a long-acting LHRH agonist preparation on plasma gonadotrophin and prolactin levels in castrated male rats and on the release of prolactin from ectopic pituitaries. Regul. Pept. 15:219–228; 1986.
39. Shiino, M.; Arimura, A.; Rennels, E. G. Effects of blinding, olfactory bulbectomy and pinealectomy on prolactin and growth hormone cells of the rat, with special reference to ultrastructure. Am. J. Anat. 139:191–198; 1975.
40. Simpkins, J. W.; Gabriel, S. M. Chronic hyperprolactinemia causes progressive changes in hypothalamic dopaminergic and noradrenergic neurones. Brain Res. 309:277–281; 1984.
41. Steger, R. W.; Bartke, A.; Goldman, B. D. Alterations in neuroendocrine function during photoperiod induced testicular atrophy and recrudescence in the golden hamster. Biol. Reprod. 26:437–444; 1982.
42. Tamarkin, L.; Westrom, W. K.; Hamil, A. I.; Goldman, B. D. Effect of melatonin on the reproductive systems of male and female hamster: diurnal rhythm in sensitivity to melatonin. Endocrinology 99:1534–1541; 1976.
43. Trancho, G. Estudio antropológico de una población meroítica sudanesa. Tesis Doctoral. Universidad Complutense, Madrid, 1986.
44. Tresguerres, J. A. F.; Esquifino, A. I. Dissociation in the regulation of luteinizing hormone annd follicle-stimulating hormone in a hyperprolactinemic rat model: Interrelationships between gonadotropin and prolactin control. J. Endocrinol. 90:41–51; 1981.
45. Tresguerres, J. A. F.; Esquifino, A. I.; Oriol-Bosch, A. Interaction between prolactin and gonadotrophin secretion. In: McKerns, L., ed. Reproductive processes and contraception. New York: Plenum Press; 1981:421–447.
46. Tresguerres, J. A. F.; Esquifino, A. I.; Pérez Méndez, L. F.; López Calderón, A. Possible role of prolactin in the inhibitory effect of oestradiol on the hypothalamic-pituitary-testicular axis in the rat. Endocrinology 108:83–87; 1981.
47. Tresguerres, J. A. F.; Esquifino, A. I. Posibles mecanismos de interacción entre gonadotropinas y prolactina en un modelo de hiperprolactinemia experimental. Acta Physiol. Pharmacol. Latinoam. 33:257–274; 1983.
48. Tresguerres, J. A. F.; Esquifino, A. I.; Calderón, A. L. Effects of estradiol benzoate and castration on LH in experimental hyperprolactinemia. J. Steroid Biochem. 19:447–453; 1983.