CHRONIC EFFECT OF TESTOSTERONE AND THYROXINE ON PLASMA AND PITUITARY LEVELS OF LH, FSH, AND PRL IN BLINDED ADULT MALE SYRIAN HAMSTERS*

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Abstract

This study observed that blinding caused significant suppression of the secretion of the gonadally related adenohypophyseal hormones as well as regression of reproductive organs in the adult male golden hamsters. The pituitary concentrations of FSH and PRL as well as the circulating levels of LH and PRL in the sightless hamsters became significantly less than the corresponding intact control value. Daily administrations of 2 µg thyroxine for 50 days further suppressed significantly both the pituitary and plasma PRL concentrations and the plasma LH level of the bilaterally orbital enucleated male hamsters. No significant changes in the plasma FSH level or in the pituitary concentrations of either LH or FSH of the blinded hamsters were observed 50 days following administrations with thyroxine alone. Administrations of solely testosterone (100 µg, every other day) or of combined testosterone and thyroxine to the blinded male hamsters caused significant suppressions on the pituitary concentration of LH but had no significant effects on either the pituitary PRL or FSH concentration. While plasma PRL and FSH levels were not significantly affected, the plasma LH level of the sightless male hamsters treated with either testosterone or combined testosterone and thyroxine was markedly suppressed below the vehicles-injected blind control level. Regarding the effect of hormone administrations on the reproductive organ weights of the blinded hamsters, it was observed that marked suppressions on the testes weights of the sightless hamsters were produced by administrations with testosterone, thyroxine, or the combined hormone treatments; and that the decline in testes weights paralleled closely the decline in plasma LH and PRL levels. While injections of thyroxine alone produced no significant change in the weight of the seminal vesicles and the coagulating glands, the weight of these accessory sex organs increased significantly above the blind control level following testosterone or combined testosterone and thyroxine treatments. Nevertheless, the weights of the accessory sex organs in the testosterone or testosterone and thyroxine treated groups, whose circulating levels of LH and PRL remain significantly depressed below intact control levels, were significantly less than the weight of these organs in the intact controls. All these results suggest that the pineal of the sightless hamster does not directly exert its effects on gonadal

regression through declining of circulating testosterone and thyroxine levels. They also provide more evidence to substantiate the view that a reduction in the release of LH, FSH and PRL are responsible for testicular regression in the light-deprived male Syrian hamsters.

Introduction

Effects of blinding or short daily photoperiods on the neuroendocrine-thyroidal and neuroendocrine-gonadal axes in hamsters have been widely investigated ¹⁻³. Briefly, light restriction in male hamsters resulted in significant decreases in 1) circulating thyroxine levels and free thyroxine index (FTI)⁴⁻⁸, 2) serum thyroid stimulating hormone (TSH)⁸⁻⁹, 3) thyroidal follicular epithelial cell height of follicles situating near the center of the gland⁸, 4) regression of the reproductive organs¹⁰⁻¹⁹, 5) circulating levels of either follicle stimulating hormone (FSH), luteinizing hormone (LH),or prolactin(PRL)^{15,17,19-23}, and in 6) pituitary levels of LH, FSH and PRL^{20,24-25}. Light restriction also led to a cessation in spermatogenesis and a decline in androgen levels in male hamsters 15-17,26 as well as a decrease in anterior pituitary weight¹¹. Moreover, light-deprived male hamsters also had increased pituitary TSH content²⁷, and increased hypothalamic content of luteinizing hormone-releasing hormone (LH-RH)²⁸ and thyrotropin-releasing hormone (TRH)²⁹. Most of these changes have been shown to involve the presence of the animal's intact pineal gland; and that they seem to be overcome by either the surgical ablation of the pineal gland, by its sympathetic denervation, or by subcutaneous melatonin implants^{1,3,27}.

The specific mechanisms involved in pineal-induced atrophy of the reproductive system under blinding or short photoperiod conditions have not been elucidated. The investigations of Bartke et al. 16, Matthews et al. 30, Bex et al. 31, and Chen and Reiter 32 have suggested that lowering of circulating levels of LH, FSH, PRL, and possibly also growth hormone (GH) are responsible for testicular regression and subsequent hypotrophy of the sex adnexa. Furthermore, it has been proposed that the antigonadotrophic hormone of the pineal gland, possibly melatonin, increases the sensitivity of the hypothalamo-pituitary unit (of the castrated hamsters) to the inhibitory feedback effects of the gonadal steroids in the secretion of LH and FSH^{2,17,33}. Could the pineal of the light-deprived animals exert its effects on gonadal regression through declining of circulating testosterone and thyroid hormone levels has not been investigated, however.

Although environmental lighting is the major input control pineal activity, hormone secreted by endocrine organs whose activity is modulated directly or indirectly by the pineal also affect the function of the gland ³⁴. As reviewed by Cardinali *et al.* ³⁵ and Mess ³⁶, experiments carried out in various animal species (rat, rabbit, sheep, cow, rhesus monkey) reveal that testosterone and other sex steroids as well as thyroid hormones can significantly alter the function and morphology of the pineal gland (by either acting directly on the gland or through functional changes in neural input to the gland).

Hence, the purpose of the present study was to investigate the role of testosterone and thyroxine on the neuroendocrine-reproductive system of the male hamsters subjected to bilateral orbital enucleation and kept under LD 14: 10 long photoperiods.

Materials and Methods

Forty-nine young adult male golden Syrian hamsters (Mesocricetus auratus) of the LAK: LVG strain, Lakeview Hamster Colony, Newfield, New Jersey, were used for this investigation. The animals were housed in a temperature controlled (22 ± 2°C) room automatically illuminated for 14 hours daily (LD 14:10) throughout the experiment. Lights were on from 6:00 AM to 8:00 PM. The light intensity at the bottom of the cages was between 40 and 50 footcandles. They were given food (Wayne Lab Blox) and drinking water ad libitum.

At 60 (between 58 and 62) days of age, nine animals were kept as the eyes-intact normal controls. The others were blinded by bilateral orbital enucleation under ether anesthesia according to the method of Reiter and Hester 11 and were divided into the following groups (of ten animals each): 1) blinded control hamsters injected subcutaneously with the vehicles (0.1 ml peanut oil and 0.1 ml normal saline made slightly basic with 0.1 N NaOH), 2) hamsters that were blinded and received subcutaneous injections of testosterone (100 µg in 0.1 ml peanut oil per injection, once every other hamsters that were blinded and received daily subcutaneous injections of thyroxine (2 µg in 0.1 ml normal saline made slightly basic with 0.1 N NaOH per injection), and 4) hamsters that were blinded and received combined injections of testosterone (100 µg, once every other day) and thyroxine (daily, 2 µg). The orbital enucleations were carried out in the morning between 9:30 and 10:45 AM. Testosterone (U.S.P., lot No. A 5581) and DL-thyroxine (M.A., lot No. F 2842) were purchased from Mann Research Laboratories, Inc., New York, N.Y. Planters Oil (100% pure peanut oil), containing no preservatives or additives was manufactured by Planters Company. The injections were made in the afternoon (between 3:00 and 3:30 PM) subcutaneously on the back. The first hormone injection was administered on the day of the operation. At the onset of the experiments, the average initial body weight of each group of hamsters was not significantly different from other groups (i.e., it ranged between 98 ± 3 g and 100 ± 4 g).

At 50 days after the operation and hormonal treatments the animals from all groups (including the eyes-intact normal controls) were sacrificed by decapitation. At this time the final body weight, the (paired) testes and the accessory sex organs (the seminal vesicles and coagulating glands), and the anterior pituitary weights were recorded. The accessory sex organs were removed and weighed without their secretions. The anterior pituitaries were quickly removed, weighed and homogenized in a total of 2.0 ml 0.05 M cold phosphate buffer. Through decapitation, trunk blood was

collected individually into heparinized tubes and centrifuged for 20 min at 3000 rpm. Plasma and pituitary samples were frozen (at-20°C) until time of assay. The autopsy was performed in the morning between 8:00 and 10:00 AM; i.e., each individual hamster from each alternate group was decapitated at every 2.4-minute intervals.

Immunoreactive plasma and pituitary LH and FSH levels were respectively estimated by the double antibody radioimmunoassay (RIA) techinques described by Goldman and Porter³⁷ and Seegal and Goldman³⁸. Pituitary and plasma levels of PRL were estimated using the double antibody RIA procedure of Donofrio *et al.*³⁹. Kits for the assays of all three hormones were supplied by the Rat Hormone Distribution Program, NIAMDD, NIH. Luteinizing hormone (LH) and FSH levels were expressed, respectively, as the equivalence of NIAMDD-Rat LH-I-4 and NIAMDD-Rat FSH-I-3. Because of lack of parallelism between rat and hamster PRL inhibition curves, hamster PRL data in this study were expressed in reference to a pool of standard hamster anterior pituitaries (SHAP) according to Donofrio *et al.*³⁹. The SHAP standard used in this study was from a different pool of that used earlier by Donofrio *et al.*³⁹. Each sample was assayed in a duplicate and the values averaged. The data were analyzed by one-way analysis of variance and t test for multiple means. The level of significance used for all data analyses was 0.05.

Results

Plasma Hormone Levels

The plasma levels of LH, FSH, and PRL are presented in Table 1.

Luteinizing Hormone — Plasma level of LH of the male hamsters was significantly suppressed 50 days following bilateral orbital enucleation ($P < 0.01 \ vs.$ intact controls). Greater suppression of plasma level of LH of the blinded hamsters was observed following administrations of testosterone alone, combined testosterone and thyroxine, and thyroxine alone (P < 0.05, P < 0.05, and P < 0.01, respectively, vs. blind controls). No statistical differences in plasma LH levels were observed among the three hormone-injected groups.

Follicle Stimulating Hormone — Plasma FSH level in the male hamsters was not significantly altered by blinding. Although there was a tendency that injections of testosterone and thyroxine, either alone or combinedly, might suppress the plasma FSH levels of the blinded male hamsters, the decline observed had not reached the level of statistically significant difference.

Prolactin — Blinding caused a significant suppression of the plasma PRL level in the male hamsters ($P < 0.05 \ vs.$ intact controls). Daily injection of thyroxine caused greater suppression of plasma PRL level (P < 0.01 and $P < 0.05 \ vs.$ intact controls and blind controls, respectively). Administrations with testosterone alone or testosterone and thyroxine had no significant effects on the plasma PRL level in blinded male hamsters.

TABLE 1. MEAN (± SE) FINAL BODY WEIGHT AND PLASMA LEVELS OF LH, FSH, AND PRL IN ADULT MALE GOLDEN HAMSTERS, AS INFLUENCED BY BLINDING WITH OR WITHOUT TESTOSTERONE (T), OR THYROXINE (T₄), OR THE COMBINED ADMINISTRATIONS FOR 50 DAYS.

Group and treatmen		Body wt	Plasma hormones			
Group and treatmen	IL II		LH (ng/ml)	FSH (ng/ml)	PRL) (μg SHAP/ml)	
I. Intact	9	115.1 ± 2.9	4.0 ± 0.1	6.2 ± 1.3	0.74 ± 0.10	
2. Blind + Vehicles	10	134.5 ± 3.2^{c}	3.2 ± 0.2^{b}	6.0 ± 0.7	0.48 ± 0.06^{a}	
3. Blind + T	10	136.9 ± 3.7^{c}	$2.8 \pm 0.1^{c,d}$	4.3 ± 0.8	0.42 ± 0.08^{a}	
1. Blind + T_4	10	135.2 ± 4.8^{b}	$2.7 \pm 0.1^{c,e}$	4.6 ± 1.0	$0.33 \pm 0.05^{b,d}$	
5. Blind + T + T_A	10	$150.3 \pm 4.8^{c,f}$	$2.8 \pm 0.1^{c,d}$	5.7 ± 1.1	0.49 ± 0.05^{a}	

SHAP, Pool of standard hamster anterior pituitaries.

 $^{^{}a}P < 0.05$ vs. intact controls (group 1).

^bP < 0.01 vs. intact controls (group 1).

 $^{^{\}rm c}P$ < 0.001 vs. intact controls (group 1).

^dP < 0.05 vs. blind controls (group 2).

 $^{^{\}rm e}{\rm P}$ < 0.01 vs. blind controls (group 2).

 $^{^{\}rm f}P$ < 0.05 vs. blind controls (group 2), blind +T (group 3), and blind +T₄ (group 4).

Pituitary Hormone Levels

The pituitary LH, FSH, and PRL concentrations are illustrated in Table 2.

Luteinizing Hormone — Blinding alone for 50 days did not significantly diminish the pituitary LH concentration of the male hamsters. Administrations of testosterone alone significantly suppressed the pituitary LH concentration ($P < 0.001 \ vs.$ both the blind controls and the intact controls). Significant depressed pituitary LH concentration was also observed in blinded hamsters injected with testosterone and thyroxine (P < 0.001 and P < 0.01, respectively, vs. the intact controls and the blind controls). While the pituitary LH concentration of the blinded hamsters injected with thyroxine alone was not significantly different from that of the blind controls, it was significantly smaller than the intact controls level (P < 0.01).

Follicle Stimulating Hormone — Blinding resulted in a significant suppression of the pituitary FSH concentration (P < 0.05 vs. intact controls). None of the hormone treatments produced any marked effects on the pituitary FSH concentration of the blinded hamsters.

Prolactin — Blinding caused a significant reduction in the pituitary PRL concentration ($P < 0.05 \ vs.$ intact controls). Injections of thyroxine alone further suppressed the pituitary PRL concentration of the blinded male hamster (P < 0.001 and $P < 0.05 \ vs.$ the intact controls and the blind controls, respectively). Injections with either testosterone alone or with a combination of testosterone and thyroxine had no significant effects on the pituitary PRL concentration of the blinded male hamsters.

Testes Weights

Data on paired testes weights of this study are shown in Fig 1. Blinding alone resulted in a singificant decrease in the weight of the testes when compared to corresponding control value. Testosterone and thyroxine, given alone or combinedly, produced a much greater decline in both the absolute and relative testes weights of the blinded hamster. Statistical analyses revealed that testicular regression in the hormone-treated blinded hamsters were similar in all three treatment groups. It should be noted that testes of the hormone(s)-treated blinded hamsters regressed more uniformly.

Accessory Sex Organ Weights

As shown in Fig. 2, blinding alone led to a significant decrease in accessory sex organ weights. While administrations of thyroxine alone had no significant effects on either the absolute or relative weight of accessory sex organs of blinded hamsters, testosterone administrations alone or in combination with thyroxine restored partially the weights of these sex adnexa (i.e. the absolute weight increased from 63% to between 82% and 85% of the normal control level; and the relative weight increased from 53% to between 64% and 70% of the normal control level). When compared to the normal control group, significant degrees of regression of the sex accessory organs were still apparent.

TABLE 2. MEAN (± SE) ANTERIOR PITUITARY (AP) WEIGHT AND PITUITARY CONCENTRATIONS OF LH, FSH, AND PRL IN ADULT MALE GOLDEN HAMSTERS, AS INFLUENCED BY BLINDING WITH OR WITHOUT TESTOSTERONE (T), OR THYROXINE (T), OR THE COMBINED ADMINISTRATIONS FOR 50 DAYS.

Group and treatment		n weig	AP	Pituitary hormonal concentrations		
			(mg)	LH (ng/mg AP)	FSH (ng/mg AP)	PRL (µg SHAP/mg AP)
	Intact Blind + Vehicles Blind + T Blind + T ₄	10	2.25 ± 0.06 2.02 ± 0.06^{a} 2.03 ± 0.06^{a} 2.20 ± 0.10		79.1 ± 9.9^{a}	146.1 ± 8.3 115.8 ± 11.1^{a} 103.2 ± 10.4^{b} $186.3 \pm 9.0^{c,d}$ 122.3 ± 9.5
	Blind + $T + T_4$	10	2.15 ± 0.07	$1,059 \pm 75^{\circ}$	$55.7 \pm 10.3^{\circ}$	$\begin{bmatrix} 00.3 \pm 9.0 \\ 122.3 \pm 9.5 \end{bmatrix}$

SHAP, Pool of standard hamster anterior pituitaries.

 $^{^{}a}P < 0.05$ vs. intact controls (group 1).

 $^{^{\}mathrm{b}}\mathrm{P}$ < 0.01 vs. intact controls (group 1).

 $^{^{\}rm C}P$ < 0.001 vs. intact controls (group 1).

 $^{^{\}rm d}P<0.05$ vs. blind controls (group 2).

 $[\]frac{e}{f}P < 0.01$ vs. blind controls (group 2).

 $_{*0}^{\text{f}}$ P < 0.001 vs. blind controls (group 2).

^{*[} P < 0.05 between pair

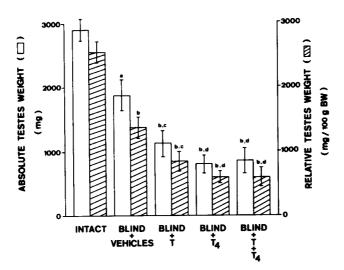


FIG. 1. Mean (\pm SE) paired absolute(\square) and relative(\square) testes weights in adult male golden hamsters, as influenced by blinding with or without testosterone (T), or thyroxine (T₄), or the combined administration for 50 days, ${}^{a}P < 0.01$, and ${}^{b}P < 0.001$, respectively, vs. intact controls; while ${}^{c}P < 0.05$, and ${}^{d}P < 0.001$, respectively, vs. vehicles-injected blind controls.

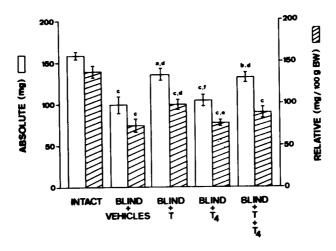


FIG. 2. Mean (\pm SE) absolute(\square) and relative(\square) accessory sex organ (seminal vesicles and coagulating glands without their secretions) weights in adult male golden hamsters, as influenced by blinding with or without testosterone (T), or thyroxine (T₄), or the combined administrations for 50 days. $^aP<0.05$, $^bP<0.01$, and $^cP<0.001$, respectively, vs. intact controls; $^dP<0.01$ vs. blind + vehicles; $^eP<0.02$, and $^fP<0.01$, respectively, vs. blind + T.

Discussion

The present investigation observed that the testes and accessory sex organs of the blinded hamsters were markedly atrophic. As referred to previously in the Introduction section of this paper ¹⁰⁻¹⁹, this is not an uncommon finding in hamster after blinding. Previous investigations had demonstrated that complete atrophy of the testes and accessory sex organs of animals in this species were obtained between 8 and 10 weeks of exposure to less than 12.5 h of light/day ¹². The present study had purposely chosen a period of about 7 weeks (50 days) to induce only partial regression of the reproductive organs with the hope that it might be able to detect any further suppressive changes that may occur with hormone treatments. Data on the testes weights and accessory sex organ weights as well as that of the gonadally related adenohypophyseal hormone levels have revealed the usefulness of such experimental design.

Results on the plasma and pituitary levels of adenohypophyseal hormones after blinding are in most parts confirmatory to those reported earlier ^{15,17,19–25,40} and have suggested that both the secretion and production of LH of the blinded male golden hamsters are significantly suppressed by administrations with testosterone or thyroxine alone or a combination of testosterone and thyroxine. Similarly, secretion as well as production of PRL in the sightless hamsters are markedly suppressed by administrations with thyroxine alone but are not significantly altered by administrations with testosterone alone or a combination of testosterone and thyroxine. When results on the testes weights are combined, it is evident that the pineal of the sightless or light-deprived hamsters does not directly exert its effects on gonadal regression through declining of cirulating testosterone and thyroid hormone levels but rather through other mechanism (s). Since the decline in the circulating LH and PRL levels of the animals correlates well with the weight of their testes, it is most likely, as proposed earlier ^{16,30–32}, that a reduction in the release of LH, FSH and PRL are responsible for testicular regression in the light-deprived male hamsters.

The effects of testosterone on growth and function of the accessory sex organs are universally accepted 41-42. This fact has also been confirmed in the present study. It was observed that administrations with testosterone alone or combined testosterone and thyroxine caused a significant elevation in the weight of the accessory sex organs in the blinded hamsters; but this dose of testosterone failed to restore the weight of these organs to the normal level in both cases. It is likely that failure of the exogenous testosterone to completely restore the weight of these organs to normal level in the present study is due primarily to the failure of either testosterone alone or combined testosterone and thyroxine to restore the circulating levels of PRL and LH (and possibly total testosterone; i.e., endogenous plus exogenous) of the blinded hamsters to normal. Studies in the rat have shown that PRL augments the testosterone-mediate growth and function of the prostate 43-44. Treatments which restore circulating PRL levels in

hamsters maintained under short day conditions markedly stimulate spermatogenic and endocrine activity of the testes as well as restore the weight of the seminal vesicles and coagulating glands through an increase in androgen productions^{16, 30-32}. As shown, circulating levels of LH and PRL in all four groups of the blinded hamsters were significantly less than the eyes-intact normal controls kept under LD 14:10 lighting regimens; thus, a smaller weight of the accessory sex organs would be encountered.

Data of the present study suggest that the production and secretion of LH (and possibly FSH) of the blinded male hamsters are greatly reduced by administrations with testosterone (either given alone or in combination with thyroxine). In the light of previous studies it is possible that testosterone produces its negative feedback effects on LH (and possibly FSH) secretion at three sites; i.e. the hypothalamus⁴⁵⁻⁴⁷, the pituitary gland⁴⁸⁻⁴⁹, and the pineal gland^{2,17,33,35-36}. The first two sites of its action are quite well established. To what extent does testosterone regulate the activity of the pineal gland³⁵⁻³⁶, whose secretion modifies the sensitivity of the hypothalamo-pituitary unit to the inhibitory feedback effects of testosterone on the secretion of LH and FSH^{2,17,33}, awaits further experimentation.

It is evident from this study that production and secretion of PRL in the blinded hamsters are significantly diminished with thyroxine administrations. How exactly does thyroxine produce this effect also requires further studies. According to the TRH hypothesis of pineal function proposed by Vriend 50, it is suspected that thyroxine does this through a reduction in the release of hypothalamic TRH.

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บทคัดย่อ

จากการศึกษาในไซเรียนโกลเดนแฮมสเตอร์เพศผู้ที่ถูกเด็ดลูกตาออกทั้งสองข้างพบว่าระดับของ FSH และ PRL concentration ในพุหน้าของต่อมใต้สมอง และระดับของพลาสมา LH และ PRL ลดลงอย่างมีนัยสำคัญจากระดับ ปกติใน 50 วันหลังจากการผ่าตัด การเด็ดลูกตาออกยังมีผลทำให้ต่อมอัณฑะ และเซมินัลเวซีกัลกับต่อมโคอักกูเลดติงผ่อ ลงด้วย การฉีดไธร็อกซีน (T_A) ปริมาณวันละ 2 ไมโครกรัมให้กับสัตว์ทดลองที่เด็ดลูกตาออกเป็นเวลา 50 วัน มีผล ทำให้ต่อมอัณฑะผ่อมากขึ้นและทำให้ระดับของ PRL concentration ในต่อมใต้สมองกับระดับพลาสมา PRL ลดลง ไปอีกเป็นอย่างมาก แต่ไม่เกิดผลที่เด่นชัดต่อระดับ LH และ FSH concentration ในต่อมใต้สมอง หรือต่อระดับพลาสมา FSH ในแฮมสเตอร์ที่ถูกเด็ดลูกตาออกแต่อย่างใด การฉีด เทสโทสเตอโรน (T) ปริมาณ 100 ไมโครกรัม วันเว้นวัน เพียงอย่างเดียว หรือการฉีด T ควบกับ T_{a} แก่แฮมสเตอร์ที่เด็ดตาออกทั้งสองข้างมีผลทำให้ต่อมอัณฑะมีน้ำหนักลด ลงไปจากระดับคอนโทรลที่เด็ดตาออก แต่จะทำให้เชมินัลเวซีกัลกับต่อมโคอักกูเลตติงโตขึ้นอย่างมีนัยสำคัญ (แต่ทั้งนี้ น้ำหนักของอวัยวะดังกล่าวยังคงเบากว่าของกลุ่มคอนโทรลตาปกติอยู่มากอย่างมีนัยสำคัญ) นอกจากนั้นการฉีด T หรือ T ควบกับ T₄ ยังมีผลทำให้ระดับ LH concentration ในต่อมใต้สมองและระดับ LH ในพลาสมาในสัตว์ทดลองทั้งสอง กลุ่มมีค่าต่ำกว่ากลุ่มคอนโทรลที่เด็ดตาออกอย่างมีนัยสำคัญอีกด้วย ผลที่ได้จากการศึกษานี้ได้บ่งชี้หรือแลดงให้เห็นได้ อย่างค่อนข้างชัดเจนว่ากลไกที่ทำให้เกิดมีการฝ่อของต่อมอัณฑะในไซเรียนแฮมสเตอร์ ที่ตาบอดนั้นไม่ได้เนื่องมาจากการ ที่มีการลดลงไปจากระดับปกติอย่างมีนัยสำคัญของปริมาณของเทสโทสเตอโรน และไธร็อกซีนในเลือด นอกจากนั้น ผลที่ได้จากการศึกษานี้ยังได้เพิ่มเติมข้อมูลที่เอื้อต่อการสนับสนุนความเห็นที่ว่าการฝ่อของต่อมอัณฑะในไชเรียนแฮม สเตอร์ตาบอด (หรือที่ถูกจำกัดปริมาณของแสงให้น้อยกว่าเกณฑ์ต้องการ) นั้นเกิดจากการที่มีการลดลงของการหลั่งของ ฮอร์โมน LH, FSH และ PRL จากต่อมใต้สมองเป็นสำคัญ