REPRODUCTIVE BIOLOGY

REVIEW

Seasonal changes in the hypothalamo-pituitary-gonadal axis in birds

Anna Leska[1], *Luiza Dusza*
Department of Animal Physiology, University of Warmia and Mazury in Olsztyn, Poland

Received: 15 February 2007; accepted: 30 June 2007

SUMMARY

Seasonal reproduction in birds is the adaptation to breed at the time of the greatest survival of young. This exact moment is mainly imposed by the photoperiod which stimulates the hypothalamo-pituitary-gonadal axis and starts breeding season. This article summarizes present knowledge concerning: 1/ perception and transduction of light into the biological signal; 2/ model of the avian photoperiodic response; 3/ seasonal changes in hypothalamic secretion of gonadotropin-releasing hormone (GnRH), vasoactive intestinal polipeptide (VIP), as well as the gonadotropin inhibitory hormone (GnIH); 4/ seasonal interactions between pituitary hormones; 5/ seasonal morphological and functional changes within the avian gonads. *Reproductive Biology 2007 7 2:99-126.*

Key words: birds, seasonal reproduction, hypothalamo-pituitary-gonadal axis

---

[1] Corresponding author: Department of Animal Physiology, University of Warmia and Mazury in Olsztyn, ul. Oczapowsiego 1A, 10-719 Olsztyn, Poland; e-mail: anna.leska@uwm.edu.pl

INTRODUCTION

Seasonal reproduction in birds ensures the hatching of young during the most favorable environmental conditions. Such conditions are determined by the availability of food, the ultimate factor directly affecting survival. Differentiated food demands restrict the breeding season to a species-specific time. Birds have to predict the time of rich food resources. This ability is under the control of endogenous circannual rhythm [29, 51] which is synchronized by periodically changing environmental factors. The seasonal changes in daylenght is the most important signal for setting the appropriate time of the year for bird reproduction. Other signals including presence of mate, nest site, social interactions, temperature or appearance of rich food supply are important for final tuning the exact moment of reproduction [30, 31, 120, 121]. In addition to these factors, the role of memory in the prediction of breeding season is proved in some species [49].

With smaller latitudes and thus with a smaller annual variation of photoperiod, birds have to integrate more supplementary cues to predict breeding season [156]. Tropical birds rely on the local climate or light intensity which informs them about coming rainfall, always followed by a period of sufficient food [59]. However, there is evidence that tropical birds respond to even minimal changes in daylength [6]. Some transequatorial and opportunistic species can breed at any time of the year with enough accessible food. They keep their reproductive system in a state of readiness throughout most of the year and are exceptionally sensitive to environmental cues [31, 59]. In general, females are more precise in the exact beginning of breeding season as their reproduction demands more energy [17].

The hypothalamo-pituitary-gonadal (HPG) axis in birds

The integrated environmental cues activate hypothalamic gonadotropin-releasing hormone (GnRH) and vasoactive intestinal polipeptide (VIP) neurons to secrete peptides which reach gonadotrophs, specific pituitary cells, through the hypophyseal portal vessels. The gonadotrophs, controlled by GnRH, release luteinizing hormone (LH) and follicle-stimulating hormone (FSH), while lactotrophs, stimulated by VIP, synthesize prolactin (PRL). Interestingly, GnRH and VIP can also directly affect gonads *via* the appropriate gonadal receptors [3, 63, 137].

Gonadotropins bind to their gonadal receptors and affect the functioning of the ovaries and testes. In females, FSH promotes gonadal maturation and follicular selection as well as regulates progesterone secretion by granulosa cells of prehierarchal follicles. LH controls estrogen and androgen production by mature ovarian follicles. In males, FSH stimulates gonadal growth and estrogen secretion by Sertoli cells. Luteinizing hormone, in turn, is responsible for androgen production by Leydig cells. Sex steroids maintain gonadal function, ensure the negative feedback on higher levels of the reproductive axis, evoke secondary sex characteristics (e.g. color and shape of plumage, growth of the comb) and impinge on sexual behavior [63, 70]. Prolactin receptors are also present in avian gonads [81, 141]. However, in contrast to FSH and LH, PRL inhibits steroidogenic enzyme gene expression [138] and reduces testis weight [15].

MEDIOBASAL HYPOTHALAMUS AS THE CENTER OF PHOTOPERIODISM

In the majority of temperate-zone birds, lengthening days activate the HPG axis at the beginning of each reproductive season. Birds are characterized by the ability to measure the daylength to match it with appropriate seasonal activities (photoperiodic time measurement). Measuring the daylength involves light perception followed by transduction of the light signal into an endocrine one. For many years scientists have looked for the structure that plays the crucial role in this phenomenon. Lesions within mediobasal hypothalamus (MBH) including infundibulum (IN), median eminence (ME) and inferior hypothalamic nucleus, conducted by Sharp in the late 1960s [122] eliminated the avian reproductive response to long days. Moreover, electrical stimulation of these areas resulted in LH secretion and testicular growth [98]. Since then, the MBH has been extensively examined and proved to be the brain region vital for photoperiodism in birds.

Photoperiodic clock

Generally birds, unlike mammals, do not use melatonin to convey photoperiodic information as the primary signal for the reproductive system [52, 65]. In some species (e.g. white crowned sparrow *zonotrichia leucophrys*, blackheaded bunting *Emberiza melanocephala*, house finch *Carpodacus mexicanus*), however, the photoperiodic clock is coupled to some extent with the circadian clock formed by the eye, pineal gland and suprachiasmatic nucleus [115]. The evidence of melatonin receptors within brain structures connected with light perception [18] and the melatonin influence on their metabolism [77] indicates a rather indirect way of pineal hormone involvement in the control of avian reproduction.

Unquestionably, the main mechanism responsible for the transmission of photoperiodic information in birds is the photoperiodic clock which consists of clock genes and is located in the MBH [160]. Avian clock gene expression is stable during various photoperiods and provides information about the daylength. It also enables birds to maintain a photosensitive phase which is important since light is effective in stimulating the reproductive axis only during this genetically encoded period of time [160]. The photosensitive phase determines the critical daylenght ("the first long day") triggering the beginning and termination of the breeding season.

It is of interest that continuous light is not required to evoke physiological changes leading to the start of the reproductive season. Experiments confirmed that only two pulses of light are sufficient to activate the avian photoperiodic response. The first pulse occurs at dawn which triggers the photoperiodic clock to begin the countdown to the start of the photosensitive phase. The second pulse has to be provided during the photosensitive phase, and initiates endocrine changes associated with reproduction [5].

Perception and transduction of light

After 50 years of research [153] we know that light detection involving retinal and pineal photoreceptors responsible for sense of sight and biological rhythms, in birds - contrary to mammals - is not associated with the activation of the reproductive axis. There is evidence that in the latter vertebrates, deep brain photoreceptors are involved in this process [87]. Photopigment rhodopsin, converting photon energy into neural impulses, was found in the avian hypothalamus [45]. Light-induced degradation of rhodopsin produces opsin, whose presence was demonstrated by immunohistochemistry in cerebrospinal fluid contacting neurons of the lateral septum (LS) and IN [116, 132, 152]. Thus, the MBH is the site of light perception important for seasonal activation of reproduction in birds.

The earliest molecular events induced by light take place in the MBH. Expression of immediate-early c-Fos genes (marker of neuronal activation) within neurons in the IN [83] and the hypothalamic tuberal area as well as within glial cells in the ME precedes the first endocrine changes associated with the HPG axis activation [91]. The GnRH and VIP neurons can be activated directly or indirectly. The direct way is linked to coexpression of opsin and VIP proteins in cells of LS and tuberal area of the hypothalamus [132]. In addition, opsin neurons form synapses on GnRH neurons [117].

The indirect transfer of photic information from the MBH to GnRH neurons occurs *via* tanycytes, specialized glial cells. Photoreceptors and glial cells are adjacent to each other (fig. 1; [163]) and photo-induced

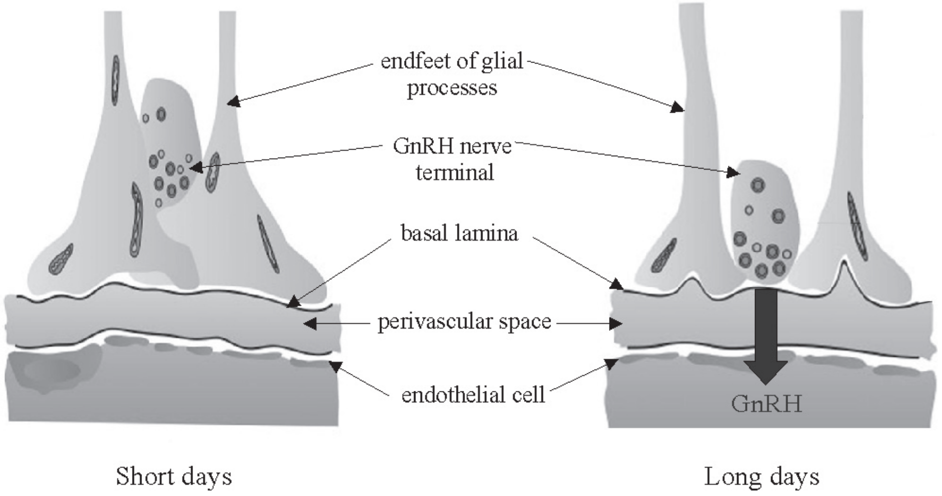

Fig. 1. Schematic morphological changes in the GnRH nerve terminals and endfeet of glial processes in the median eminence under short and long days (modified from Yoshimura [163])

reactions influence the activity of glial cells [48, 117]. Photoreceptor-activation by “the first long day” affects tanycyte transcription of two enzymes genes: it up-regulates transcription of 2 iodothyronine deiodinase (Dio2; [164]) and down-regulates 3 deiodinase (Dio3; [161]). Dio2 converts prohormone thyroxine (T4) to bioactive triiodothyronine (T3) while Dio3 turns both T3 and T4 into inactive metabolites [161]. The contradictory effects exerted by the long photoperiod on the transcription of these two genes increase the brain level of T3 about 10-fold in photostimulated birds. The locally produced T3 acts - *via* thyroid hormone receptors - on glial cells in the ME and IN. This results in a retraction of glial endfeet which enables the GnRH neuronal terminals to come closer to the perivascular space to release GnRH [159, 164]. In contrast to long days, the pattern of Dio2 and Dio3 expression during short days eliminates the high level of T3, and glial cells block the GnRH neuron connection again with the basal lamina [161].

The second, thyroid-independent, pathway for photoperiodic regulation of reproduction involves long-day induced transcription of transforming growth factor alpha (TGFα) gene within the MBH. Experiments checked that TGFα intracerebroventricular infusion conducted even during short days increased plasma LH and evoked testicular growth. This is successive evidence that TGFα is involved in the control of seasonal reproduction in birds but the exact mechanism of its action has to be elucidated [139].

Model of the photoperiodic response for avian long-day breeders

In addition to the main pathway of controlling avian seasonal reproduction, involving the photoperiodic clock described in the previous subchapter, a constant activity of genotype-dependent stimulatory input to GnRH and VIP neurons occurs in birds. The constitutive, genotype-dependent stimulation sustains only basal activity of GnRH and VIP neurons and is overriden by the stronger and photoperiodically controlled biological clock [95, 124].

As the spring progresses (fig. 2B; [124]) the length of day light reaches a critical threshold, triggering the activation of two types of inputs to GnRH and VIP neurons. The stimulatory input responds rapidly to the critical

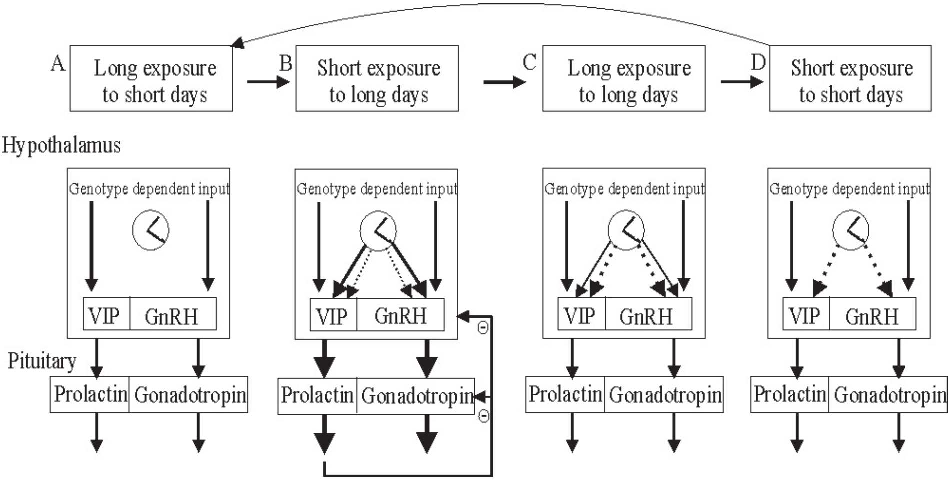

Fig. 2. Model of the avian neuroendocrine photoperiodic reproductive response for long-day breeders, incorporating a role for prolactin. The levels of inputs and outputs in the neuroendocrine system are indicated by the thickness of the lines and arrows: continuous lines-stimulation, broken lines-inhibition; for description see on pages 104–106 and 111–112 (from Sharp and Blache [124] for National Research Council Canada permission)

changes in daylength. The stimulation of the GnRH neurons (followed by a maximal activation of VIP neurons [123]) results in gonadotropin release and gonadal activation. The response to the inhibitory input develops more slowly thereby having little effect during breeding season [124].

As days get longer, the critical daylength for termination the breeding season is reached and the stimulatory input diminishes. At the same time, the inhibitory input to GnRH and VIP neurons increases and begins to predominate over the stimulatory one (fig. 2C; [124]). Despite the ongoing long photoperiod, the hypothalamus becomes refractory to light [31, 33, 34]. This dual effect of long days (stimulatory or not - depending on a time of year) controls the asymmetry of the breeding season. Such asymmetry enables birds to rear their young and molt before severe weather conditions. The majority of middle and high latitude species are absolute photorefractory because their reproductive quiescence cannot be broken by any photoperiod including constant light [30, 31, 33]. In contrast, in species exhibiting a relative photorefractoriness e.g. Japanese quail (*Coturnix japonica*), the terminated reproductive activity may be restored by exposure to daylength longer than that which triggered the termination of reproduction [21].

Exposure to short days is required to overcome both types of photorefractoriness. The gradual decrease in inhibitory input occurring during short days leads to the recovery of hypothalamic photosensitivity to light (fig. 2D; [124]). During long exposure to short days, GnRH and VIP neurons are not activated by the photoperiodic clock (fig. 2A; [124]) and genotype stimulation of GnRH and VIP neurons becomes significant. The latter notion is supported by moderate increase in LH during late fall and early winter observed in domestic geese (*Anser anser f. domestica*) or house sparrows (*Passer domesticus*) [56, 60]. The LH increase results in slow gonadal activation enabling preparations for breeding season e.g. winter courtship, mating and establishment of nest sites [53, 121]. Genotype dependent stimulation is thus very important for developing optimal breeding strategies [120].

SEASONAL PLASTICITY IN THE HYPOTHALAMIC SYSTEM CONTROLLING GONADOTROPIN SECRETION

GnRH types: structure, distribution and ability to stimulate gonadotropin secretion

The GnRH is a decapeptide stimulating gonadotropin secretion which is synthesized in hypothalamic neurons. Up to now three types of GnRH (tab. 1) and two types of GnRH receptor [130, 137] have been found in the avian brain. The domestic chicken was the first vertebrate species in which two distinct forms of GnRH (cGnRH-I and cGnRH-II) were sequenced [67, 92]. First GnRH-III was demonstrated in lamprey and recently it was also found in the brain of songbirds [8]. The three GnRH types differ in structure, distribution and function.

The main population of cGnRH-I cell bodies is located in the preoptic area (POA) with fibers extending along the third ventricle and finally entering the ME, a hypothalamic area of GnRH secretion [46, 88]. The

Table 1. Amino acid sequence of avian GnRH isoforms

cGnRH-I	**pGlu-His-Trp-Ser**-Tyr-Gly-Leu-Gln-**Pro-Gly-NH2**
cGnRH-II	**pGlu-His-Trp-Ser**-His-Gly-Trp-Tyr-**Pro-Gly-NH2**
GnRH-III	**pGlu-His-Trp-Ser**-His-Asp-Trp-Lys-**Pro-Gly-NH2**

Bold typing represents amino acids in the conserved NH2- and COOH-terminals

presence of cGnRH-II in the ME and thus its involvement in the control of reproduction is controversial. Several researches reported the presence of cGnRH-II fibers in the ME [26, 143, 151] and cGnRH-II release from the ME [90], but always in a smaller amount than cGnRH-I. However, others did not confirm this information [85, 86]. Chicken GnRH-II neurons, on the other hand, are more widely distributed in other brain areas, especially in the midbrain [89]. In addition, GnRH-III neurons are also widespread in the central nervous system of birds, particularly in the telencephalon (hippocampus and song control areas; [8]).

The three forms of GnRH differ in their ability to release gonadotropins. All of them, although to different extents, stimulate secretion of LH [8, 106]. The potency of cGnRH-I and cGnRH-II was found to be either comparable to each other [58] or the GnRH types differed in their *in vitro* or *in vivo* actions [50, 69, 106, 126]. cGnRH-I is thought, however, to be the main hypophysiotropic factor stimulating the release of LH since active immunization against cGnRH-I, but not cGnRH-II, caused a decline in plasma LH and complete regression of the reproductive system [128]. On the other hand, seasonal changes in the cGnRH-II cell immunoreactivity suggest an involvement of cGnRH-II in the control of reproduction [136, 143]. The critical role of cGnRH-II in the stimulation of female courtship behavior has also been proved [79]. Moreover, the widespread brain abundance of cGnRH-II and GnRH-III suggests their functional significance. cGnRH-II may act as neurotransmitter [64] and GnRH-III as a potential mediator in transducing song-related stimuli to areas controlling gonadotropin secretion [8].

The influence of the GnRH on FSH secretion is not fully elucidated. In contrast to other researchers [42, 75, 106], Hattori and Ishi [58] found that cGnRH-I and cGnRH-II stimulate *in vitro* and *in vivo* FSH release. A constitutive release of FSH [57] and distinct localization of FSH and LH-producing cells in bird pituitaries [105] suggest that FSH secretion may not be closely associated with GnRH stimulation. Discrete regulatory mechanisms may be involved in the secretion of the two gonadotropins in birds. The photoinduced release of FSH may involve a regulatory role of ovarian follistatin and activin, which stimulates and inhibits FSH expression, respectively. The follistatin synthesis, decreased under lower GnRH pulse frequency, may be responsible for an increased FSH level [42].

Seasonal changes in GnRH-I content and secretion

Changes in the activity of hypothalamic cGnRH-I neurons are the key events in the avian seasonal neuroendocrine response [31]. The synthesis of cGnRH-I in the POA is resumed during short days i.e. when birds regain photosensitivity. However, the rate of cGnRH-I release is too low then to stimulate gonadal growth. GnRH synthesis elevates approximately three-fold as daylength increases. Subsequent higher secretion of cGnRH-I stimulates gonadal maturation [32, 36, 46]. The highest brain level of GnRH mRNA and peptide was detected during full breeding conditions [23, 35, 41, 46, 66, 93, 128, 143].

Inhibited cGnRH-I secretion is the first step towards ending reproductive activity [86]. When photorefractoriness starts, cGnRH-I synthesis is still maintained and no changes in the cGnRH-I content are observed in the POA neurons [84, 86]. At the end of the breeding season, in the relative photorefractory Japanese quail, cGnRH-I secretion stops but cGnRH-I continues to be synthesized and the peptide accumulates in the brain [47, 143]. In contrast, longer exposure to long days leads to reduced GnRH synthesis in absolute photorefractory birds [23, 34, 46, 54, 66]. At this time there is a dramatic, about 100-fold, decline in hypothalamic cGnRH-I level [35] in comparison with reproductively active birds. In the opportunistic breeders, flexible regulation of reproduction is characterized by tonic activation of GnRH neurons which may take place even after decreased activity of the pituitary and gonads [102].

It should be emphasized that, in addition to GnRH amount, the effect of GnRH depends on receptor availability [69, 130]. It is of interest that the expression of the cGnRH-II receptor (cGnRH-IIR) increases in photostimulated birds which indicates cGnRH-IIR involvement in the control of reproduction [130].

Control of GnRH-I secretion

Photoperiod is the main regulator of the activity of GnRH neurons [124], and other cues like access to food [13, 25] or local tropical climate [39, 93] play an important though supplemental role. The combined environmental factors activate the HPG axis: the GnRH stimulates pituitary release of gonadotropin, which, in turn, increases gonadal production of steroid hormones. An increasing level of sex steroids exerts a negative feedback on the GnRH system. Gonadectomy increases hypothalamic synthesis of GnRH and pituitary release of LH [73]. Testosterone, in turn, decreases the number of immunoreactive cGnRH-I cells in the POA and cGnRH-I fibers in the ME [38, 73]. Similarly, estrogens depress cGnRH-I mRNA and peptide concentrations in the POA and cGnRH-I receptor in the pituitary of juvenile cockerels. In adult males, the inhibitory role of gonadal estrogens is replaced by brain androgen aromatization [40, 137].

Hypothalamic VIP is also thought to inhibit GnRH expression [36]. It was revealed that VIP receptor mRNA and peptide co-exist with cGnRH-I cells and fibers in the LS and caudalmost septal area [20, 144]. Furthermore, an electron microscopy study has shown synaptic connections between VIP axons and GnRH cell bodies or dendrites in the lateral septal-preoptic area [71].

The delayed, in comparison to GnRH, maximal photoperiodic activation of VIP neurons enables the VIP-ergic system to inhibit GnRH after the annual peak of the latter is reached [124]. Thus, there is an inverse relationship between VIP and GnRH peptide content in the MBH at the beginning of the photorefractoriness period [36] and it lasts as the period progresses [112, 126]. Experimental immunoneutralization of VIP is followed by a significant increase in pituitary content of LHβ and FSHβ mRNAs accompanied by a decline in PRL mRNA expression [1]. PRL acts synergistically with VIP inhibiting LH by means of reduction of GnRH level in the hypothalamus [114].

A gonadotropin-inhibitory hormone (GnIH; dodecapeptide) is another factor affecting GnRH secretion [146]. Increased GnIH expression at the end of the breeding season [7, 24] is induced by elevated melatonin level during a short photoperiod. Melatonin appears to act directly since GnIH neurons are equipped with melatonin receptors [147]. Expression of GnIH receptor mRNA was found in the quail diencephalon, in the ME close to cGnRH-I fiber terminals [9] as well as in the pituitary [162]. These results suggest the existence of a second site of GnIH action i.e. pituitary. GnIH inhibited LH and FSH synthesis and release *in vitro* [24]. This was confirmed by *in vivo* GnIH injections which resulted in decreased expression of LHα and β subunit mRNAs, plasma LH, testosterone and spermatogenic activity. The decrease in the HPG axis activity led to testicular apoptosis [148]. GnIH is widely distributed in the diencephalic and mesencephalic areas which indicates it participates not only in the regulation of the neuroendocrine function but also in the regulation of behavior [149]. Centrally injected GnIH inhibited female sexual behavior possibly by inhibiting the cGnRH-II neuronal activity [9]. The ultimate suppression of the GnRH activity is derived from biological clock which triggers inhibitory input to GnRH neurons (fig. 2; [124]).

SEASONAL CHANGES IN PITUITARY HORMONES

Annual changes in gonadotropin levels

A photoperiodic treshold responsible for an increase in FSH spring secretion is reached earlier than that of LH [135]. Then the gradual increase in plasma FSH is observed. The period of elevated FSH encompasses the time of nest building, gonadal development and lasts till the end of breeding season [53, 76, 134]. Plasma FSH level is found to be higher in males than in females and in paired birds compared to single birds [135]. Moreover, in the great tit (*Parus major*) for example, there is a second annual peak of FSH which occurs during the autumnal break of photorefractoriness [134].

The photoinduced LH increase is sudden and, compared to FSH, delayed [95, 135]. Plasma LH level peaks during the laying period [50, 56, 158]. The negative feedback of gonadal steroids plays an important role in controlling LH level during the breeding cycle. Ovariectomy results in a higher level of pituitary LHβ and α subunit mRNAs and this increase is reversed by exogenous estrogens [142]. Gonadal steroids suppress basal [154] and GnRH-induced [27] plasma LH. Moreover, the estrogen negative feedback on the hypothalamus and pituitary [107, 113] was blocked in tamoxifen (antiestrogen)-treated birds. Gonadal steroid feedback, however, is insufficient to initiate a significant LH decline which coincides with the appearance of photorefractoriness [28, 96].

The LH inhibition at the onset of photorefractoriness is caused by an enhanced plasma PRL level [31, 33, 43, 80, 99]. As photorefractoriness advances the PRL level decreases and cannot be responsible for inhibition of LH [33]. Photoperiodic inhibition of GnRH neurons plays a major role in maintaining the depressed LH level during photorefractoriness [41]. In addition to short days, in the Japanese quail, a low temperature is also involved in the ultimate decline in LHβ mRNA [74].

The role of PRL in photoperiodic response

The critical daylength, similar for LH and PRL release, results in their initial parallel secretion. Maximal PRL response, however, requires longer photoperiod than that of LH [129]. Additionally, during the laying phase, PRL inhibits its own secretion by decreasing hypothalamic VIP content and pituitary VIP receptors [114]. These mechanisms maintain low PRL and maximal LH level during breeding season.

When PRL photoperiodic response is maximal, PRL inhibits plasma LH which results in regression of gonads at the beginning of photorefractoriness [31, 33, 35, 43, 80, 99, 125]. The inhibitory mode of PRL action includes hypothalamus and the pituitary gland (fig. 2B). PRL injections reduced hypothalamic cGnRH-I, cGnRH-II and plasma LH [114] as well as inhibited the steroidogenic effect of FSH and LH on the ovary [16, 138]. These findings are supported by results of *in vitro* experiments in which PRL down-regulated LHβ gene expression and inhibited LH release [165]. The PRL antigonadotropic activity leads to the inverse ratio of LHβ and PRL mRNA levels in laying and incubating birds [158].

In birds, PRL is considered to be a parental care hormone [43]. A high plasma PRL level and/or an elevated sensitivity of PRL receptors in the POA and LS are characteristic for both incubating females and males [14, 43]. PRL secretion can be enhanced by nesting behavior [43, 110] or tactile stimuli from eggs [12, 55]. The increased PRL level during egg incubation [43, 97, 140] is due to several mechanisms including photoperiod (fig. 2B; [124]) and, especially in females, estrogenic activation of VIP neurons [72].

Multiple factors are capable of influencing the VIP-ergic neuron activity. The dynorphin-serotonin-dopamine pathway contributes to VIP and consequently PRL release [168, 169, 170]. VIP enhances both transcription and stability of PRL mRNA [145]. The serotonin binding sites were increased in the anterior hypothalamus of incubating hens [78]. Dopamine (DA) acts *via* hypothalamic/pituitary D1 (stimulation of VIP/PRL secretion) and D2 receptors (inhibition of VIP/PRL secretion). In incubating birds, the up-regulation of hypothalamic D1 receptor is correlated with increased pituitary mRNA PRL expression and plasma PRL level [11, 168]. Moreover, the high PRL level during the incubating stage is also accompanied by down-regulation of hypothalamic and pituitary D2 receptors [2, 19, 119]. In addition, at this time PRL does not exert a negative feedback on hypothalamic VIP neurons and pituitary VIP receptors [114]. In incubating birds, the high VIP mRNA and peptide content [127, 166] is positively correlated with VIP mRNA receptors at the pituitary level [20].

The high PRL level found in incubating birds is associated with anatomical changes of pituitary cells. In this stage, lactotrophs recruit from mammosomatotrophs, become hypertrophic and extend from the cephalic to the caudal lobe of the pituitary [108, 109, 118]. Physical contact with chicks induces transition from incubating to brooding behavior associated with decreased PRL and increased LH secretion, rapid in the presence of precocial and slower of altricial young [111]. The definitive decline in PRL in photorefractory birds [19, 35, 43] is due to VIP-ergic neuron inhibition by the photoperiodic clock [129].

SEASONAL FLUCTUATIONS IN GONADAL MORPHOLOGY AND FUNCTIONS

Factors affecting gonadal development

In temperate latitudes, daylength is the most important factor affecting the initiation of gonadal growth, but it is not sufficient to end this process. Many supplementary cues influence later stages of gonadal maturation. They are also needed for expressing reproductive behavior and physiology. The sensitivity to these additional signals is genetically encoded and differs among particular populations of the same species [101].

Food accessibility is one of the major mediators of environmental conditions required for gonadal development and breeding commencement. Birds fed *ad libitum* had an increased number of large preovulatory ovarian follicles and full-size testis [10, 25].

Temperature, another environmental factor, appears to also modulate gonadal growth. This is especially visible in females since they put more effort in reproduction than males and have to eliminate the risk of breeding prematurely. Gonadal maturation of females is divided into two phases. The first one is controlled by photoperiod and allows the immature ovary to reach the developmental stage of 2-3 mm follicles [68]. A rapid deposition of yolk followed by ovulation and oviposition occurring during the second phase of gonadal maturation appears when environmental conditions become favorable [155].

Low temperatures can inhibit the reproductive system *via* elevated corticosterone levels [131]. Since corticosterone decreases fat accumulation and lowers body mass, its enhanced level causes delays in vernal migration of females which have to arrive at breeding grounds in their best condition [157]. On the other hand, high temperatures can accelerate gonadal growth. This is probably mediated by elevated PRL levels, whose release is known to be stimulated by high temperatures. At the beginning of breeding season, PRL may act as a progonadal factor increasing the number of gonadotropin receptors in gonads [33, 80].

In addition, social interactions in birds play crucial role for synchronizing reproductive actions between a male and a female. In ring doves (*Streptopelia decaocto*), male courtship induces nest-coo display in females and stimulates ovarian growth by audio- and proprioceptive feedback [22]. Follicular development in the willow tit (*Parus montanus*) is also more progressive in the presence of the opposite sex [133].

Seasonal changes in gonadal steroid levels

Mature gonads secrete sex steroid hormones. Androgens, estrogens and progestagens present in circulation bind to corticosterone binding protein (CBG), a plasma transporting protein, with different affinity. Steroid binding to CBG regulates bioavailability of the hormones. Both, photoperiod and testosterone affect CBG level and control plasma amounts of free steroids [37]. Other supplementary cues, including social stimulation by a partner, can also modulate seasonal hormone fluctuations. The social stimulation induces a pronounced hormonal profile in both sexes [61].

Androgens (e.g. testosterone) produced by theca interna cells of ovarian follicles and testicular Leydig cells contribute to rapid gonadal maturation in response to photostimulation [38, 39]. Plasma testosterone (T) peak coincides with territorial behavior of males [150] and the highest quality of sperm production [100]. In both sexes, T stimulates sexual behavior and its annual maximal level is observed during the mating period [61]. After a decline in photorefractoriness at the beginning of the autumnal postrefractory period, a second T peak is observed in some species. The second T peak is a demonstration of gradual gonadal development characteristic for spontaneous sexual reactivation [56, 61, 62, 99]. In addition, T probably participates in preparing the reproductive tract for the approaching mating season. It also regulates social interactions and is important in food competition behavior.

Estrogens are produced by theca externa cells in females and by Sertoli cells in males [61]. Pairing activity is associated with elevated estrogen level. Estrogens are required for ovarian development which in turkey hens diminishes after tamoxifen treatment [107]. In female domestic geese with no offspring, in which the social status is lower than that of females with offspring, estrogens started to rise earlier in the year, displayed higher amplitude and remained elevated for a longer time compared to females with breeding success. In the unsuccessful females, the enhanced estrogen level might help to deposit more fat and to better prepare them for the next breeding season [61]. These data support the notion concerning a relationship between social status and hormone levels.

Progesterone, the main progestagen secreted by the largest follicle, exerts a positive feedback on hypothalamus stimulating the preovulatory LH surge. The first preovulatory LH peak is followed by a breeding season with repeated cycles of ovulation and oviposition [63].

Sex steroids exert their negative feedback usually on both pituitary and hypothalamus levels [27, 40, 107, 137, 142, 154]. The inhibitory effect of steroids on the reproductive axis is insufficient in initiating the photorefractoriness [28]. The start of photorefractoriness requires a combined action of PRL and prolonged exposure to long days [31, 33, 35, 43, 80, 99, 125]. It cannot also be excluded that melatonin, due to its gonadal receptors, is another factor involved in the appearance of refractoriness and gonadal regression [4].

Gonadal regression occurs at the beginning of incubation period, when ovarian steroids act synergistically with PRL in LH depression [44, 103]. Regression of testes is mediated by apoptosis of germ and somatic (Sertoli and Leydig) cells [167]. The degenerated Leydig cells become fibroblast-like structures which in future breeding seasons turn into a new generation of juvenile interstitial cells [94]. In females, follicular atresia starts at the beginning of the egg incubation period and concerns the largest preovulatory F1 follicle first and then within the next three days extends from the F2 to F7 follicle [103].

The amplitude of annual fluctuations in gonadal function and morphology is spectacular in birds. Thanks to dramatic seasonal alterations in gonadal weight (up to a hundred-fold), birds are perfectly well adapted to the challenge of long flight migration.

CONCLUSIONS

The knowledge of avian endocrinology allows us to describe the particular steps of the bird reproductive response to changes in photoperiod: 1/ light perceived by photoreceptors in the MBH stimulates GnRH and VIP neurons activity directly or *via* surrounding glial cells; 2/ the main hypophysiotropic GnRH-I peptide entails a cascade of physiological changes resulted in gonadal growth and expression of full breeding conditions; 3/ multiple regulatory mechanisms are involved in the inhibition of GnRH neuron activity (VIP, PRL, steroid feedback loop and increasing during short days level of GnIH); 4/ the inhibitory inputs from the biological clock finally contribute to the loss of hypothalamic sensitivity to light, which means photorefractoriness manifested in regression of gonads and molt; 5/ a period of exposure to short days leads to recovery of the hypothalamic photosensitivity to light which enables the next breeding season to be started.

However, the constant development of advanced laboratory techniques is the key to learning further details of the complicated reproductive regulatory mechanisms. The recently examined involvement of GnIH and thyroid hormones, not described in this review [82, 104], in the avian seasonal reproduction can fulfill our knowledge about it. Many interactions at all levels of the reproductive axis have to be explained to better understand the phenomenon of seasonal reproduction.

ACKNOWLEDGEMENTS

This work was supported by the project No. 0206.0805 of the Ministry of science and Higher Education, Poland and the European Social Funds (for AL).

REFERENCES

1. Ahn J, You S, Kim H, Chaiseha Y, el Halawani ME **2001** Effects of active immunization with inhibin alpha subunit on reproductive characteristics of turkey hens. *Biology of Reproduction* **65** 1594-1600.
2. Al Kahtane A, Chaiseha Y, el Halawani ME **2003** Dopaminergic regulation of avian prolactin gene transcription. *Journal of Molecular Endocrinology* **31** 185-196.
3. Asem EK, Novero RP **1993** Chicken gonadotropin-releasing hormones enhances soluble and insoluble fibronectin production by granulosa cells of the dometic fowl in vitro. *Poultry Science* **72** 1961-1971.
4. Ayre EA, Pang SF **1994** 2-[125] iodomelatonin binding sites in the tesis and ovary: putative melatonin receptors in the gonads. *Biological Signals* **3** 71-84.
5. Ball GF, Balthazart J **2003** Birds return every spring like clockwork, but where is the clock? *Endocrinology* **144** 3739-3741.

6. Bentley GE, Spar BD, MacDougall-Shackleton SA, Hahn TP, Ball GF **2000** Photoperiodic regulation of the reproductive axis in male zebra finches, Taeniopygia guttata. *General and Comparative Endocrinology* **117** 449-455.
7. Bentley GE, Perfito N, Ukena K, Tsutsui K, Wingfield JC **2003** Gonadotropin- inhibitory peptide in song sparrows (Melospiza melodia) in different reproductive conditions, and in house sparrows (Passer domesticus) relative to chicken gonadotropin- releasing hormone. *Journal of Neuroendocrinology* **15** 794-802.
8. Bentley GE, Moore IT, Sower SA, Wingfield JC **2004** Evidence for a novel gonadotropin-releasing hormone in hypothalamic and forebrain areas in songbirds. *Brain, Behavior and Evolution* **63** 34-46.
9. Bentley GE, Jensen JP, Kaur GJ, Wacker DW, Tsutsui K, Wingfield JC **2006** Rapid inhibition of female sexual behavior by gonadotropin-inhibitory hormone (GnIH). *Hormones and Behavior* **49** 550-555.
10. Bhardwaj SK, Anushi N **2004** The effect of duration and time of food availability on the photoperiodic response in the male house sparrow, Passer domesticus. *Reproduction, Nutrition, Development* **44** 29-35.
11. Bhatt R, Youngren O, Kang S, el Halawani ME **2003** Dopamine infusion into the third ventricle increases gene expression of hypothalamic vasoactive intestinal peptide and pituitary prolactin and luteinizing hormone beta subunit in the turkey. *General and Comparative Endocrinology* **130** 41-47.
12. Book CM, Millam JR, Guinan MJ, Kitchell RL **1991** Broodpatch innervation and its role in the onset of incubation in the turkey hen. *Physiology and Behavior* **50** 281-285.
13. Bruggeman V, D'Hondt E, Berghman L, Onagbesan O, Vanmontfort D, Vandesande F, Decuypere E **1998** The effect of food intake from 2 to 24 weeks of age to LHRH-I content in the median eminence and gonadotrophin levels in pituitary and plasma in female broiler breeder chickens. *General and Comparative Endocrinology* **112** 200-209.
14. Buntin JD, el Halawani ME, Ottinger MA, Fan Y, Fivizzani AJ **1998** An analysis of sex and breeding stage differences in prolactin binding activity in brain and hypothalamic GnRH concentration in Wilson's Phalarope, a sex role-reversed species. *General and Comparative Endocrinology* **109** 119-132.
15. Buntin JD, Advis JP, Ottinger MA, Lea RW, Sharp PJ **1999** An analysis of physiological mechanisms underlying the antigonadotropic action of intracranial prolactin in ring doves. *General and Comparative Endocrinology* **114** 97-107.
16. Camper PM, Burke WH **1977** The effects of prolactin on the gonadotropin induced rise in serum estradiol and progesterone in the laying turkey. *General and Comparative Endocrinology* **32** 72-77.
17. Caro SP, Lambrechts MM, Chastel O, Sharp PJ, Thomas DW, Balthazar J **2006** Simultaneous pitiutary-gonadal recrudescence in two Corsican populations of male blue tits with asynchronous breeding dates. *Hormones and Behavior* **50** 347-360.
18. Cassone VM, Brooks DS, Kelm TA **1995** Comparative distribution of 2[^{125}I]iodomelatonin binding in the brains of diurnal birds: outgroup analysis with turtles. *Brain, Behavior and Evolution* **45** 241-256.
19. Chaiseha Y, Youngren O, Al-Zailaie K, el Halawani ME **2003** Expression of D1 and D2 dopamine receptors in the hypothalamus and pituitary during the turkey reproductive cycle: colocalization with vasoactive intestinal peptide. *Neuroendocrinology* **77** 105-118.
20. Chaiseha Y, Youngren OM, el Halawani ME **2004** Expression of vasoactive intestinal peptide receptor messenger RNA in the hypothalamus and pituitary troughout the turkey reproductive cycle. *Biology of Reproduction* **70** 593-599.

21. Chaturvedi CM, Bhatt R, Philips D **1993** Photoperiodism in Japanese quail with special reference to relative refractoriness. *Indian Journal of Experimental Biology* **31** 417-421.
22. Cheng MF, Desiderio C, Havens M, Johnson A **1988** Behavioral stimulation of ovarian growth. *Hormones and Behavior* **22** 388-401.
23. Cho RN, Hahn TP, MacDougall-Shackleton S, Ball GF **1998** Seasonal variation in brain GnRH in free-living breeding and photorefractory house finches (Carpodacus mexicanus). *General and Comparative Endocrinology* **109** 244-250.
24. Ciccone NA, Dunn IC, Boswell T, Tsutsui K, Ubuka T, Ukena K, Sharp PJ **2004** Gonadotrophin inhibitory hormone depresses gonadotrophin alpha and follicle- stimulating hormone beta subunit expression in the pituitary of the domestic chicken. *Journal of Neuroendocrinology* **16** 999-1006.
25. Ciccone NA, Dunn IC, Sharp PJ **2006** Increased food intake stimulates GnRH-I, glycoprotein hormone alpha-subunit and follistatin mRNAs, and ovarian follicular numbers in laying broiler breeder hens. *Domestic Animal Endocrinology*, article in press.
26. Clerens S, D`Hondt E, Berghmen LR, Vandesande F, Archens L **2003** Identification of cGnRH-II in the median eminence of Japanese quail *(Coturnix coturnix japonica)*. *General and Comparative Endocrinology* **131** 48-56.
27. Connolly PB, Callard IP **1987** Steroids modulate the release of luteinizing hormone from quail pituitary cells. *General and Comparative Endocrinology* **68** 466-472.
28. Dawson A **1984** Effects of gonadectomy on seasonal changes in plasma LH and prolactin concentrations in male and female starlings (Sturnus vulgaris). *Journal of Neuroendocrinology* **100** 213-218.
29. Dawson A **1997** Plasma luteinizing hormone and prolactin during circannual rhythms of gonadal maturation and molt in male and female European starlings. *Journal of Biological Rhythms* **12** 371-377.
30. Dawson A **1999** Seasonal reproduction, Birds. *Encyclopedia of Reproduction* **4** 321-328.
31. Dawson A **2001** Photoperiodic control of seasonality in birds. *Journal of biological rhythms* **16** 365-380.
32. Dawson A, Goldsmith AR **1997** Changes in gonadotrophin-releasing hormone (GnRH-I) in the preoptic area and median eminence of starlings (Sturnus vulgaris) during the recovery of photosensitivity and during photostimulation. *Journal of Reproduction and* Fertilit*y* **111** 1-6.
33. Dawson A, Sharp PJ **1998** The role of prolactin in the development of reproductive photorefractoriness and postnuptial molt in the European starling (Sturnus vulgaris). *Endocrinology* **139** 458-490.
34. Dawson A, Goldsmith AR, Nicholls TJ, Follet BK **1986** Endocrine changes associated with the termination of photorefractoriness by short day lenghts and thyroidectomy in starlings *(Sturnus vulgaris)*. *Journal of Endocrinology* **110** 73-79.
35. Dawson A, Talbot RT, Dunn IC, Sharp PJ **2002** Changes in basal hypothalamic chicken gonadotropin-releasing hormone-I and vasoactive intestinal polypeptide associated with a photo-induced cycle in gonadal maturation and prolactin secretion in intact and thyroidectomized starlings (Sturnus vulgaris). *Journal of Neuroendocrinology* **14** 533-539.
36. Deviche P, Saldanha CJ, Silver R **2000** Changes in brain gonadotropin-releasing hormone- and vasoactive intestinal polypeptide-like immunoreactivity accompanying reestablishement of photosensitivity in male dark-eyed juncos (Junco hyemalis). *General and Comparative Endocrinology* **117** 8-19.
37. Deviche P, Breuner C, Orchinik M **2001** Testosterone, corticosterone, and photoperiod interact to regulate plasma levels of binding globulin and free steroid hormone in dark-eyed juncos, Junco hyemalis. *General and Comparative Endocrinology* **122** 67-77.

38. Deviche P, Martin RK, Small T, Sharp PJ **2006** Testosterone induces testicular development but reduces GnRH-I fiber density in the brain of the House Finch, Carpodacus mexicanus. *General and Comparative Endocrinology* **147** 167-174.
39. Deviche P, Small T, Sharp P, Tsutsui K **2006** Control of luteinizing hormone and testosterone secretion in a flexibly breeding male passerine, the Rofous-winged Sparrow, Aimophila carpalis. *General and Comparative Endocrinology* **149** 226-235.
40. Dunn IC, Sharp PJ **1999** Photo-induction of hypothalamic gonadotrophin releasing hormone-I mRNA in the domestic chicken: a role for estrogen? *Journal of Neuroendocrinology* **11** 371-375.
41. Dunn IC, Beattie KK, Maney D, Sang HM, Talbot RT, Wilson PW, Sharp PJ **1996** Regulation of chicken gonadotropin- releasing hormone-I mRNA in incubating, nest- deprived and laying bantam hens. *Neuroendocrinology* **63** 504-513.
42. Dunn IC, Lewis PD, Wilson PW, Sharp PJ **2003** Acceleration of maturation of FSH and LH responses to photostimulation in prepubertal domestic hens by oestrogen. *Reproduction* **126** 217-225.
43. el Halawani ME, Burke WH, Dennison PT **1980** Effect of nest-deprivation on serum turkey prolactin level in nesting female turkeys. *Biology of Reproduction* **23** 118-123.
44. el Halawani ME, Silsby JL, Foster LK, Rozenboim I, Foster DN 1**993** Ovarian involvement in the supression of the luteinizing hormone in the incubating turkey (Meleagris gallopavo). *Neuroendocrinology* **58** 35-41.
45. Foster R, Follet BK, Lythgoe JN **1985** Rhodopsin-like sensitivity of extraretinal photoreceptors mediating the photoperiodic response in quail. *Nature* **313** 50-52.
46. Foster RG, Plowman G, Goldsmith AR **1987** Immunohistochemical demonstration of marked changes in the LHRH system of photosensitive and photorefractory European starlings *(Sturnus vulgaris)*. *Journal of Endocrinology* **115** 211-220.
47. Foster R, Panzica GC, Parry DM, Viglietti- Panzica C **1988** Immunocytochemical studies on the LH-RH system of the Japanese quail: Influence by photoperiod and aspects of sexual differentiation. *Cell and Tissue Research* **253** 327-335.
48. Gereben B, Pachucki A, Kollar A **2004** Ontogenic redistribution of type 2 deiodinase messenger ribonucleic acid in the brain of the chicken. *Endocrinology* **145** 3619-3625.
49. Grieco F, van Noordwijk AJ, Visser ME **2002** Evidence for the effect of learning on timing of reproduction in blue tits. *Science* **296** 136-138.
50. Guemene D, Williams JB **1999** LH responses to chicken luteinizing hormone- releasing hormone I and II in laying, incubating, and out of lay turkey hens. *Domestic Animal Endocrinology* **17** 1-15.
51. Gwinner E **2003** Circannual rhythms in birds. *Current Opinion in Neurobiology* **13** 770-778.
52. Gwinner E, Hau M, Heigl S **1997** Melatonin: Generation and modulation of avian circadian rhythms. *Brain Research Bulletin* **44** 439-444.
53. Haase E, Sharp PJ, Paulke E **1985** Seasonal changes in the concentrations of plasma gonadotropins and prolactin in wild mallard drakes. *Journal of Experimental Zoology* **234** 301-305.
54. Hahn TP, Ball GF **1995** Changes in brain GnRH associated with photorefractoriness in house sparrows (Passer domesticus). *General and Comparative Endocrinology* **l 99** 349-363.
55. Hall MR, Goldsmith AR **1983** Factors affecting prolactin secretion during breeding and incuabtion in the domestic duck (Anas platyrhynchos). *General and Comparative Endocrinology* **49** 270-276.
56. Hargitai CS, Forgo V, Mezes M, Dong X, Peczely P **1993** Seasonal and circadian fluctuations of plasma LH level and its change in the domestic geese as an effect of GnRH treatment. *Acta Biologica Hungarica* **44** 255-268.

57. Hattorii A, Ishii S, Wada M **1986** Different mechanisms controlling FSH and LH release in Japanese quail (Coturnix coturnix japonica): evidence for an inherently spontaneous release and production of FSH. *Journal of Endocrinology* **108** 239-245.
58. Hattori A, Ishii S, Wada M **1986** Effects of two kinds of chicken luteinizing hormone releasing hormone (LHRH), mammalian LHRH, and its analogs on the release of LH and FSH in Japanese quail and chickens. *General and Comparative Endocrinology* **64** 446-455.
59. Hau M **2001** Timing of breeding in variable environments: tropical birds as a model system. *Hormones and behavior* **40** 281-290.
60. Hegner RE, Wingfield JC **1986** Gonadal development during autumn and winter in house sparrow. *Condor* **88** 96-278.
61. Hirschenhauser K, Mostl E, Kotrschal K **1999** Seasonal patterns of sex steroids determined from feces in different social categories of Greylag geese (Anser anser). *General and Comparative Endocrinology* **114** 67-79.
62. Hirschenhauser K, Mostl E, Peczely P, Wallner B, Dittami J, Kotrschal K **2000** Seasonal relationship in plasma and fecal testosterone in response to GnRH in domestic ganders. *General and Comparative Endocrinology* **118** 262-272.
63. Johnson AL **2000** Reproduction in the female. In *Sturkie's Avian Physiology*, pp 569-596. Eds Whittow CG. Academic Press, London.
64. Jones SW **1987** Chicken II luteinizing hormone-releasing hormone inhibits the M-current of bullfrog sympathetic neurons. *Neuroscience Letters* **80** 180-184.
65. Juss T, Meddle SM, Servant RS, King VM **1993** Melatonin and photoperiodic time measurement in Japanese quail (Coturnix coturnix japonica). Proceedings*: Biological Sciences* **254** 21-28.
66. Kang SW, Thayananuphat A, Rozenboim I, Millam JR, Proudman JA, el Halawani ME **2006** Expression of hypothalamic GnRH-I mRNA in female turkey at different reproductive states and following photostimulation. *General and Comparative Endocrinology* **146** 86-94.
67. King JA, Millar RP **1982** Structure of chicken hypothalamic luteinizing hormone-releasing hormone. I. Structural determination on partially purified material. *Journal of Biological Chemistry* **257** 10722-10728.
68. King JR, Follet BK, Farner DS, Morton ML **1966** Annual gonadal cycles and pituitary gonadotrophin in Zonotrichia leucophrys gambelii. *Condor* **68** 476-487.
69. King JA, Davidson JS, Millar RP **1988** Interaction of endogenous chicken gonadotrophin-releasing hormone-I and -II on chicken pituitary cells. *Journal of Endocrinology* **117** 43-49.
70. Kirby JD, Froman DP **2000** Reproduction in male birds. In *Sturkie's Avian Physiology*, pp 597-615. Eds Whittow CG. Academic Press, London.
71. Kiyoshi K, Kondoh M, Hirunagi K, Korf H **1998** Confocal laser scanning and electron-microscopic analyses of the relationship between VIP-like and GnRH-like-immunoreactive neurons in the lateral septal-preoptic area of the pigeon *Cell and Tissue Research* **293** 39-46.
72. Knapp TR, Fehrer SC, Silsby JL, Porter TE, Behnke EJ, el Halawani ME **1988** Gonadal steroid modulation of basal and vasoactive intestinal polypeptide- stimulated prolactin release by turkey anterior pituitary cells. *General and Comparative Endocrinology* **72** 226-236.
73. Knight PG, Cunningham FJ, Gladwell RT **1983** Concentrations of immunoractive luteinizing hormone releasing hormone in discrete brain regions of the cockerel: effects of castration and testosterone replacement therapy. *Journal of Endocrinology* **96** 471- 480.
74. Kobayashi M, Ito T, Ishii S, Wada M **2004** Seasonal changes in luteinizing hormone subunit mRNA in Japanese quail and effects of short daylenght and low temperature. *General and Comparative Endocrinology* **139** 38-47.

75. Krishnan KA, Proudman JA, Bolt DJ, Bahr JM **1993** Development of an homologous radioimmunoassay for chicken follicle stimulating-hormone and measurement of plasma FSH during the ovulatory cycle. *Comparative Biochemistry and Physiology* **105** 729-734.
76. Lewis PD, Perry GC, Morris TR, Douthwaite JA **1999** Effect of timing and size of photoperiod change on plasma FSH concentration and the correlation between FSH and age at the first egg in pullets. *British Poultry Science* **40** 380-384.
77. Lu J, Cassone VM **1993** Pineal regulation of circadian rhythms of 2-deoxy[^{14}C]glucose uptake and 2[^{125}I]iodomelatonin binding in the visual system of the house sparrow, *Passer domesticus*. *Journal and Comparative Physiology* **173** 765-774.
78. Macnamee MC, Sharp PJ **1989** The functional activity of hypothalamic 5- hydroxytryptamine neurones in broody bantam hens. *Journal of Endocrinology* **120** 125-134.
79. Maney DL, Richardson RD **1997** Central administration of chicken gonadotropin- releasing hormone-II enhances courtship behavior in a female sparrow. *Hormones and Behavior* **32** 11-18.
80. Maney DL, Hahn TP, Schoech SJ, Sharp PJ, Morton ML, Wingfield JC **1999** Effects of ambient temperature on photo-induced prolactin secretion in three subspecies of white- crowned sparrow, Zonotrichia leucophrys. *General and Comparative Endocrinology* **113** 445-456.
81. Mao JN, Burnside J, Li L, Tang J, Davolos C, Coqburn LA **1999** Characterization of unique truncated prolactin receptor transcripts, corresponding to the intracellular domain, in the tesis of the sexually mature chicken. *Endocrinology* **140** 1165-1174.
82. McNabb FM **2007** The hypothalamic-pituitary-thyroid (HPT) axis in birds and its role in bird development and reproduction. *Critical Reviews in Toxicology* **37** 163-193.
83. Meddle SL, Follett BK **1997** Photoperiodically driven changes in fos expression within the basal tuberal hypothalamus and median eminence of Japanese quail. *Journal of Neuroscience* **15** 8909-8918.
84. Meddle SL, Maney DL, Wingfield JC **1999** Effects of *N*-methyl-D aspartate on luteinizing hormone release and fos-like immunoreactivity in the male White-crowned Sparrow (*Zonotrichia leucophrys gambelii*). *Endocrinology* **140** 5922-5928.
85. Meddle SL, Bush S, Sharp PJ, Millar RP, Wingfield JC **2006** Hypothamlamic pro-GnRH-GAP, GnRH-I and GnRH-II during the onset of photorefractoriness in the white-crowned sparrow (Zonotrichia leucophrys gambelii). *Journal of Neuroendocrionology* **18** 217-26.
86. Meddle SL, Wingfield JC, Millar RP, Deviche PJ **2006** Hypothalamic GnRH-I and its precursor during photorefractoriness onset in free-living male Dark-eyed Juncos (Junco hyemalis) of different year classes. *General and Comparative Endocrinology* **145** 148-156.
87. Menaker M, Roberts R, Elliott J, Underwood H **1970** Extraretinal light perception in the sparrow: 3. The eye do not participate in photoperiodic photoreception. *Proceedings of the National Academy of Sciences of the United States of America* **67** 320-325.
88. Millam JR, Faris PL, Youngren OM, el Halawani ME, Hartman BK **1993** Immunohistochemical localization of chicken gonadotropin-releasing hormones I and II (cGnRH I and II) in turkey hen brain. *Journal of Comparative Neurology* **333** 68-82.
89. Millam JR, Craig-Viet CB, Faris PL **1995** Concentration of chicken gonadotropin-releasing hormones I and II in microdissected areas of turkey hen brain during the reproductive cycle. *Domestic Animal Endocrinology* **12** 1-11.
90. Millam JR, Ottinger MA, Craig- Veit CB, Fan Y, Chaiseha Y, el Halawani ME **1998** Multiple forms of GnRH are released from perifused medial basal hypothalamic/ preoptic area (MBH/POA) explants in birds. *General and Comparative Endocrinology* **111** 95-101.
91. Millam JR, Craig-Veit CB, Siopes TD **2003** Photostimulated fos-like immunoreactivity in tuberal hypothalamus of photosensitive vs. photorefractory turkey hens. *General and Comparative Endocrinology* **134** 175-181.

92. Miyamoto K, Hasegama Y, Nomura M, Igarashi M, Kangawa K, Matsuo H **1984** Identification of the second gonadotropin-releasing hormone in chicken hypothalamus: evidence that gonadotropin secretion is probably controlled by two distinct gonadotropin-releasing hormones in avian species. *Proceedings of the National Academy of Sciences of the United States of America* **81** 3874-3878.
93. Moore IT, Bentley GE, Wotus C, Wingfield JC **2006** Photoperiod-independent changes in immunoreactive brain gonadotropin-releasing hormone (GnRH) in a free-living, tropical bird. *Brain, Behavior and Evolution* **69** 37-44.
94. Mori JG, George JC **1978** Seasonal histological changes in the gonads, thyroid and adrenal of the Canada goose (Branta canadensis interior). *Acta anatomica* **101** 304-324.
95. Nicholls TJ, Follet BK, Robinson JE **1983** A photoperiodic response in gonadectomized quail exposed to a single long day. *Journal of Endocrionology* **97** 121-126.
96. Nicholls TJ, Goldsmith AR, Dawson A **1988** Photorefractoriness in birds in comparison with mammals. *Physiological Reviews* **68** 133-76.
97. Ohkubo T, Tanaka M, Nakashima K, Sharp PJ **1998** Relationship between prolactin receptor mRNA in the anterior pituitary gland and hypothalamus and reproductive status in male and female bantams (Gallus domesticus). *General and Comparative Endocrinology* **111** 167-176.
98. Ohta M, Wada M, Homma K **1984** Induction of rapid testicular growth in Japanese quail by phasic electrical stimulation of the hypothalamic photosensitive area. *Journal of Comparative Physiology* **154** 583-589.
99. Peczely P, el Halawani ME, Hargitai CS, Mezes M, Forgo V, Janosi SZ **1993** The photorefractoriness in the domestic goose: effect of gonads and thyroid on the development of postbreeding prolactinemia. *Acta Biologica Hungarica* **44** 329-352.
100. Penfold LM, Wildt DE, Herzog TL, Lynch W, Ware L, Derrickson SE, Monfort SL **2000** Seasonal patterns of LH, testosterone and semen quality in the Northern pintail duck (Anas acuta). *Reproduction, Fertility and Development* **12** 229-235.
101. Perfito N, Meddle SL, Tramontin AD, Sharp PJ, Wingfield JC **2005** Seasonal gonadal recrudescence in song sparrows: Response to temperature cues. *General and Comparative Endocrinology* **143** 121-128.
102. Perfito N, Bentley G, Hau M **2006** Tonic activation of brain GnRH immunoreactivity despite reduction of peripheral reproductive parameters in opportunistically breeding zebra finches. *Brain, Behavior and Evolution* **67** 123-134.
103. Porter TE, Silsby JL, Behnke EJ, Knapp TR, el Halawani ME **1991** Ovarian steroid production in vitro during gonadal regression in the turkey. I. Changes associated with incubation behavior. *Biology of Reproduction* **45** 581-586.
104. Proudman JA, Siopes TD **2006** Potential role of thyroid hormones and prolactin in the programming of photorefractoriness in turkey hens. *Poultry Science* **85** 1457-1461.
105. Proudman JA, Vandesande F, Berghman LR **1999** Immunohistochemical evidence that follicle-stimulating hormone and luteinizing hormone reside in separate cells in the chicken pituitary. *Biology of Reproduction* **60** 1324-1328.
106. Proudman JA, Scanes CG, Johannsen SA, Berghman LR, Camp MJ **2006** Comparison of the ability of the three endogenous GnRHs to stimulate release of follicle- stimulating hormone and luteinizing hormone in chickens. *Domestic Animal Endocrinology* **31** 141-153.
107. Ramesh R, Proudman JA, Keunzel W **1995** Changes in pituitary somatotrophs and lactotrophs associated with ovarian regression in the turkey hen (Meleagris gallopavo). *Comparative Biochemistry and Physiology* **112** 327-334.
108. Ramesh R, Proudman JA, Kuenzel WJ **1996** Changes in pituitary somatotroph and lactotroph distribution in laying and incubating turkey hens. *General and Comparative Endocrinology* **104** 67-75.

109. Ramesh R, Solow R, Proudman JA, Kuenzel WJ **1998** Identification of mammosomatotrophs in the turkey hen pituitary: increased abundance during hyperprolactinemia. *Endocrinology* **139** 781-786.
110. Ramesh R, Kuenzel WJ, Proudman JA **2001** Increased proliferative activity and programmed cellular death in the turkey hen pituitary gland following interruption of incubation behavior. *Biology of Reproduction* **64** 611-618.
111. Richard-Yris MA, Sharp PJ, Wauters AM, Guemene D, Richard JP, Foraste M **1998** Influence of stimuli from chicks on behavior and concentrations of plasma prolactin and luteinizing hormone in incubating hens. *Hormones and Behavior* **33** 139-148.
112. Rozenboim I, Silsby JL, Tabibzadeh C, Pitts GR, Youngren OM, el Halawani ME **1993** Hypothalamic and posterior pituitary content of vasoactive intestinal peptide and gonadotropin-releasing hormones I and II in turkey hen. *Biology of Reproduction* **49** 622-626.
113. Rozenboim I, Snapir N, Arnon E, Aryeh B, Burke WH, Sharp PJ **1993** Precocious puberty in tamoxifen treated cockerels: hypothalamic gonadotropin- releasing hormone-I and plasma luteinizng hormone, prolactin, growth hormone and testosterone. *British Poultry Science* **34** 533-542.
114. Rozenboim I, Tabibzadeh C, Silsby JL, el Halawani ME **1993** Effect of ovine prolactin administration on hypothalamic vasoactive intestinal peptide (VIP), gonadotropin releasing hormone I and II content and anterior pituitary VIP receptors in laying turkey hens. *Biology of Reproduction* **48** 1246-1250.
115. Saiovici MS, Nicholls TJ, Follett BK **1987** Rapid photoperiodic responses in Japanese quail: Is daylenght measurement based upon a circadian system? *Journal of Biological Rhythms* **2** 139-152.
116. Saldanha CJ, Leak RK, Silver R **1994** Detection and transduction of daylenght in birds. *Psychoneuroendocrinology* **19** 641-656.
117. Saldanha C, Silverman AJ, Silver R **2001** Direct innervation of GnRH neurons by encephalic photoreceptors. *Journal of biological rhythms* **16** 39-49.
118. Scanes CG, Jeftinija S, Glavaski-Joksimovic A, Proudman J, Aramburo C, Anderson LL **2005** The anterior pituitary gland: Lessons from livestock. *Domestic Animal Endocrinology* **29** 23-33.
119. Schnell SA, You S, el Halawani ME **1999** D1 and D2 dopamine receptor messenger ribonucleic acid in brain and pituitary during the reproductive cycle of the turkey hen. *Biology of Reproduction* **60** 1378-1383.
120. Sharp PJ **1996** Strategies in avian breeding cycle. *Animal Reproduction Science* **42** 505-513.
121. Sharp PJ **2005** Photoperiodic regulation of seasonal breeding in birds. *Annals of the New York Academy of Sciences* **1040** 189-199.
122. Sharp PJ, Follet BK **1969** The effect of hypothalamic lesions on gonadotrophin release in Japanese quail. *Neuroendocrinology* **5** 205-218.
123. Sharp PJ, Sreekumar KP **2001** Photoperiodic control of prolactin secretion. In *Avian Endocrinology*, pp 245-255. Eds Dawson A, Chaturvedi CM. Narosa, New Delhi.
124. Sharp PJ, Blache D **2003** A neuroendocrine model for prolactin as the key mediator of seasonal breeding in birds under long- and short-day photoperiods. *Canadian Journal of Physiology and Pharmacology* **81** 350-358.
125. Sharp PJ, Klandorf H, McNeilly AS **1986** Plasma prolactin, thyroxine, triiodothyronine, testosterone, and luteinizing hormone during a photoinduced reproductive cycle in mallard drakes. *Journal of Experimental Zoology* **238** 409-413.
126. Sharp PJ, Sterling RJ, Milton RC, Millar RP **1986** Effect of luteinizing hormone releasing hormone and its analogues on plasma luteinizing hormone concentrations in incubating bantam hens. *British Poultry Science* **27** 129-135.

127. Sharp PJ, Sterling RJ, Talbot RT, Huskisson NS **1989** The role of hypothalamic vasoactive intestinal polypeptide in the maintenance of prolactin secretion in incubating bantam hens: observations using passive immunization, radioimmunoassay and immunohistochemistry. *Journal of Endocrinology* **122** 5-13.
128. Sharp PJ, Talbot RT, Main GM, Dunn IC, Fraser HM, Huskisson NS **1990** Physiological roles of chicken LHRH-I and -II in the control of gonadotrophin release in the domestic chicken. *Journal of Endocrinology* **124** 291-299.
129. Sharp PJ, Dawson A, Lea RW **1998** Control of luteinizing hormone and prolactin secretion in birds. *Comparative Biochemistry and Physiology* **119** 275-282.
130. Shimizu M, Bedecarrats GY **2006** Identification of a novel pituitary-specific chicken gonadotropin-releasing hormone receptor and its splice variants. *Biology of Reproduction* **75** 800-808.
131. Siegel HS **1980** Physiological stress in birds. *BioScience* **30** 529-534.
132. Silver R, Witkovsky P, Horvath P, Alones V, Barnstable CJ, Lehman MN **1988** Coexpression of opsin- and VIP-like immunoreactivity in CFS-contacting neurons of the avian brain. *Cell and Tissue Research* **253** 189-198.
133. Silverin B, Westin J **1995** Influence of the opposite sex on photoperiodically induced LH and gonadal cycles in willow tit (Parus montanus). *Hormones and Behavior* **29** 207-215.
134. Silverin B, Kikuchi M, Ishii S **1997** Seasonal changes in follicle-stimulating hormone in free-living great tits. *General and Comparative Endocrinology* **108** 366-373.
135. Silverin B, Kikuchi M, Ishii S **1999** Effect of season and photoperiod on FSH in male great tits. *General and Comparative Endocrinology* **113** 457-463.
136. Stevenson TJ, MacDougall-Shackleton SA **2005** Season- and age-related variation in neural cGnRH-I and cGnRH-II immunoreactivity in house sparrows (Passer domesticus). *General and Comparative Endocrinology* **143** 33-39.
137. Sun YM, Dunn IC, Baines E, Talbot RT, Illing N, Millar RP, Sharp PJ **2001** Distribution and regulation by oestrogen of fully processed and variant transcripts of gonadotropin releasing hormone I and gonadotropin releasing hormone receptor mRNAs in the male chicken. *Journal of Neuroendocrinology* **13** 37-49.
138. Tabibzadeh C, Rozenboim I, Silsby JL, Pitts GR, Foster DN, el Halawani ME **1995** Modulation of ovarian cytochrome P450 17α-hydroxylase and cytochrome aromatase messenger ribonucleic acid by prolactin in the domestic turkey. *Biology of Reproduction* **52** 600-608.
139. Takagi T, Yamamura T, Anraku T, Yasuo S, Nakao N, Watanabe M, Iigo M, Ebihara S **2007** Involvement of TGF{alpha} in the photoperiodic regulation of reproduction in birds. *Endocrinology* [article in press].
140. Talbot RT, Hanks MC, Sterling RJ, Sang HM, Sharp PJ **1991** Pituitary prolactin messenger ribonucleic acid levels in incubating and laying hens: effects of manipulating plasma levels of vasoactive intestinal polypeptide. *Endocrinology* **129** 496-502.
141. Tanaka M, Maeda K, Okubo T, Nakashima K **1992** Double antenna structure of chicken prolactin receptor deduced from the cDNA sequence. *Biochemical and Biophysical Research Communications* **188** 490-496.
142. Terada O, Shimada K, Saito N **1997** Effect of estradiol replacement in ovariectomized chickens on pituitaty LH concentrations and concentrations of mRNAs encoding LHβ and α subunits. *Journal of Reproduction and Fertility* **111** 59-64.
143. Teruyama R, Beck MM **2000** Changes in immunoreactivity to anti- cGnRH-I and -II are associated with photostimulated sexual status in male quail. *Cell and Tissue Research* **300** 413-426.

144. Teruyama R, Beck MM **2001** Double immunocytochemistry of vasoactive intestinal peptide and cGnRH-I in male quail: photoperiodic effects. *Cell and Tissue Research* **303** 403-414.
145. Tong Z, Pitts GR, You S, Foster DN, el Halawani ME **1998** Vasoactive intestinal peptide stimulates turkey prolactin gene expression by increasing transcription rate and enhancing mRNA stability. *Journal of Molecular Endocrinology* **21** 259-266.
146. Tsutsui K, Saigoh E, Ukena K, Teranishi H, Fujisawa Y, Kikuchi M, Ishii S, Sharp PJ **2000** A novel hypothalamic peptide inhibiting gonadotropin release. *Biochemical and Biophysical Research Communications* **275** 661-667.
147. Ubuka T, Bentley GE, Ukena K, Wingfield JC, Tsutsui K **2005** Melatonin induces the expression of gonadotropin-inhibitory hormone in the avian brain. *Proceedings of the National Academy of Sciences of the United States of America* **102** 3052-3057.
148. Ubuka T, Ukena K, Sharp PJ, Bentley GE, Tsutsui K **2006** Gonadotropin-inhibitory hormone inhibits gonadal development and maintenance by decreasing gonadotropin synthesis and release in male quail. *Endocrinology* **147** 1187-1194.
149. Ukena K, Ubuka T, Tsutsui K **2003** Distribution of a novel avian gonadotropin- inhibitory hormone in the quail brain. *Cell and Tissue Research* **312** 73-79.
150. van Duyse E, Pinxten R, Eens M **2003** Seasonal fluctuations in plasma testosterone levels and diurnal song activity in free-living male great tits. *General and Comparative Endocrinology* **15** 1-9.
151. van Gils J, Absil P, Grauswels L, Moons L, Vandesande F, Balthazart J **1993** Distribution of luteinizimg hormone-releasing hormones I and II (LHRH-I and -II) the quail and chicken brain as demonstrated with antibodies directed against synthetic peptides. *Journal of Comparative Neurology* **334** 304-323.
152. Wada Y, Okano T, Adachi A, Ebihara S, Fukada Y **1998** Identification of the rhodopsin in the pigeon deep brain. *FEBS Letters* **425** 53-56.
153. Wilson FE **1991** Neither retinal nor pineal photoreceptors mediate photoperiodic control of seasonal reproduction in American tree sparrows *(Spizella arborea)*. *Journal of Experimental Zoology* **259** 117-121.
154. Wilson SC, Knight PG, Cunningham FJ **1983** Evidence for the involvement of central conversion of testosterone to oestradiol-17β in the regulation of luteinizing hormone secretion in the cockerel. *Journal of Endocrinology* **99** 301-310.
155. Wingfield JC, Farner DS **1993** Endocrinology of reproduction in wild species. In *Avian biology*, pp 163-327. Eds Farner DS, King JR, Parkes KC. Academic Press, New York.
156. Wingfield JC, Hahn TP, Levin R, Honey P **1993** Environmental predictability and control of gonadal cycles in birds. *Journal of Experimental Zoology* **261** 214-231.
157. Wingfield JC, Hahn TP, Wada M, Astheimer LB, Schoech S **1996** Interrelationship of day lenght and temperature on the control of gonadal development, body mass, and fat score in white-crowned sparrows, Zonotrichia leucophrys gambelii. *General and Comparative Endocrinology* **101** 242- 255.
158. Wong EA, Silsby JL, Ishii S, el Halawani ME **1992** Pituitary luteinizing hormone and prolactin messenger ribonucleic acid levels are inversely related in laying and incubating turkey hens. *Biology of Reproduction* **47** 598-602.
159. Yamamura T, Hirunagi K, Ebihara S, Yoshimura T **2004** Seasonal morphological changes in the neuro-glial interaction between GnRH nerve terminals and glial endfeet in Japanese quail. *Endocrinology* **145** 4264-4267.
160. Yasuo S, Watanabe M, Okabayashi N, Ebihara S, Yoshimura T **2003** Circadian clock genes and photoperiodism: comprehensive analysis of clock gene expression in the mediobasal

hypothalamus, the suprachiasmatic nucleus, and the pineal gland of Japanese quail under various light schedules. *Endocrinology* **144** 3742-3748.

161. Yasuo S, Watanabe M, Nakao N, Takagi T, Follet BK, Ebihara S, Yoshimura T **2005** The reciprocal switching of two thyroid hormone activating and inactivating enzyme genes is involved in the photoperiodic gonadal response of Japanese quail. *Endocrinology* **146** 2551-2554.
162. Yin H, Ukena K, Ubuka T, Tsutsui K **2005** A novel G protein-coupled receptor for gonadotropin-inhibitory hormone in the Japanese quail (Coturnix japonica): identification, expression and binding activity. *Journal of Endocrinology* **184** 257-266.
163. Yoshimura T **2004** Molecular bases for seasonal reproduction in birds. *Journal of Poultry Science* **41** 251-258.
164. Yoshimura T, Yasou S, Watanabe M, Yamamura T, Hirunagi K, Ebihara S **2003** Light-induced hormone conversion of T4 to T3 regulates photoperiodic response of gonads in birds. *Nature* **426** 171-181.
165. You S, Foster LK, Silsby JL, el Halawani ME, Foster DN **1995** Sequence analysis of the turkey LH beta subunit and its regulation by gonadotrophin releasing hormone and prolactin in cultured pituitary cells. *Journal of Molecular Endocrinology* **14** 117-129.
166. You S, Silsby JL, Farris J, Foster DN, el Halawani ME **1995** Tissue-specific alternative splicing of turkey preprovasoactive intestinal peptide messenger ribonucleic acid, its regulation and correlation with prolactin secretion. *Endocrinology* **136** 2602-2610.
167. Young KA, Ball GF, Nelson RJ **2001** Photoperiod-induced testicular apoptosis in European starlings (Sturnus vulgaris). *Biology of Reproduction* **64** 706-713.
168. Youngren OM, Pitts GR, Philiphs RE, el Halawani ME **1996** Dopaminergic control of prolactin secretion in the turkey. *General and Comparative Endocrinology* **104** 225-230.
169. Youngren OM, Chaiseha Y, el Halawani ME **1998** Serotonergic stimulation of avian prolactin secretion requires an intact dopaminergic system. *General and Comparative Endocrinology* **112** 63-68.
170. Youngren OM, Pitts GR, Chaiseha Y, el Halawani ME **1999** An opioid pathway in the hypothalamus of the turkey that stimulates prolactin secretion. *Neuroendocrinology* **70** 317-323.