



Photoperiodic physiology of summer breeding birds and a search for the role of eye

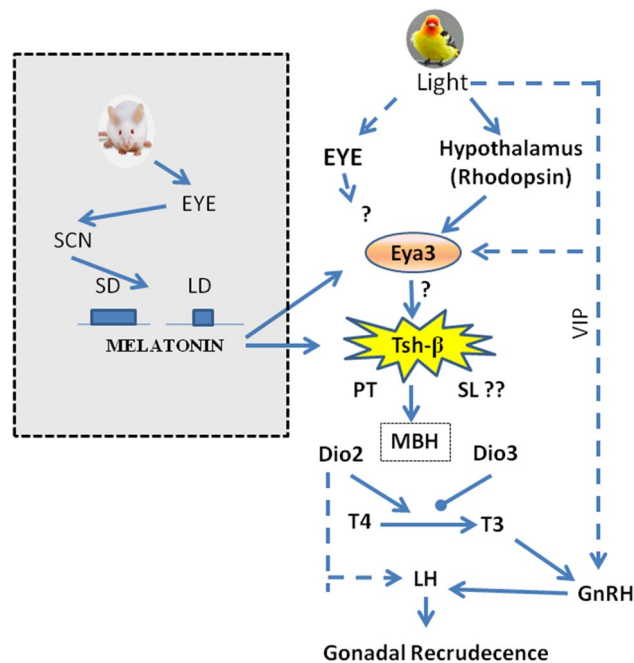
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Abstract

Photoperiod regulation of gonadal cycles is well studied and documented in both birds and mammals. Change in photoperiod is considered as the most effective and important cue to time the initiation of the annual physiological cycles in birds. Approaching of long days (as observed in summer months), signal long-day breeding birds to initiation reproduction and other related functions. Birds and other non-mammalian vertebrates use the extraocular photoreceptors which may be present in the mediobasal hypothalamus (MBH) or associated regions to measure the photoperiodic time and so are different from mammals where only the eyes are lone photoreceptive organs. The downstream signaling involves thyroid responsive genes playing a crucial role in mediating photoperiodic signals in both birds and mammals. Role of eyes in the avian seasonal cycle has been a questionable issue with evidences both favoring and negating any role. We propose that morphological as well as physiological data argue that retinal photoreceptors can participate in gonadal cycle, at least in the quail and duck. The present review details the studies of photoneuroendocrine control of gonadal axis in birds and review evidences to decipher the role eyes in photoperiodic mediated physiologies in birds.

Graphical Abstract



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Extended author information available on the last page of the article

Keywords Eye · Hypothalamus · Photoperiod · Reproduction · Thyroid

1 Introduction

In birds, the annual cycle comprises all the physiological, behavioral, and morphological adjustments that characterize its life cycle in a year [23]. Various life-history stages (LHS) that occur each year include breeding, nestling/ fledgling, molt, migration (in a migratory species), and non-breeding (refractoriness). Investigations have essentially demonstrated that change in photoperiod (seasonally in nature) and other supplementary factors induce the circulating levels of gonadotropins and sex hormones [72], ultimately resulting in the realization of the seasonal gonadal cycle. Thus, for many species of birds that inhabit regions with significant changes in daylength across the year, the photoperiod acts as a *Zeitgeber* (time giver; referring to the environmental variables capable of acting as cues to time biological clocks), persuading the development of the reproductive system to a near-functional state somewhat in advance of the mean optimal time for production of young [35, 36]. Different life-history stages have evolved in response to environmental changes. These LHSs although are the direct result of the extrinsic environmental condition, but their regulation involves intrinsic physiological mechanisms. In context, changing daylength modulates a range of intrinsic factors ranging from genes to hormones producing a visible phenotypic result. Extensive research now has clarified how the long days influence the hypothalamo-gonadal axis, leading to gonadal development [37, 38]. Importantly, non-visual photopigments with extraocular anatomy have been shown to mediate the induction and regulation of the seasonal gonadal cycle of lower vertebrates like cyclostomes, fishes, and birds along with reptiles [126]. Search for the extraretinal photoreceptors became evident when even enucleated, and pinealactomized European minnows showed normal color changes [43]. Evidence accumulated from many other species like eels [125] and many species of birds established beyond doubt the role of extraretinal photoreception in the activation of the reproductive axis. Extraretinal sites of photoreception include iris, skin, tissues like heart and kidney, and of course the brain [86]. It has also been well established that in birds (and some lower vertebrates), eyes are not involved in photoperiodic responses in terms of gonadal recrudescence [122]. As it was recently demonstrated that bird's retina also responds to changes in photoperiod [66], we conducted an in-depth search of published research revealing some interesting findings as to how eyes have some role to play in the photoperiodic regulation of seasonal cycles in birds. In this review, the intent is to

assess the literature on photoperiodic mechanisms with a bias toward studies that show the involvement of eyes.

2 The avian photoneuroendocrine system

An endogenous photoperiodic clock allows a bird to recognize the time when to start (photoinduction) and stop (photorefractoriness) its internal mechanisms, to synchronize physiological and/or behavioral events with the most suitable time of the year. Although differs between animal groups, the basic plan of photoperiodic neuroendocrine control of gonadal cycle involves (i) photoreception, (ii) integration or processing of light information, and (iii) reproductive output in the form of gonadal development.

2.1 The opsins

Structurally, almost all the opsins consist of a single polypeptide chain of 340–500 amino acids forming seven alpha-helical transmembrane regions. The transmembrane regions are connected by cytoplasmic and extracellular loops and domains. Moreover, the seven helices form bundle inside the membrane, thus creating a cavity on the extracellular side where ultimately, the retinal chromophore binds [85]. The vitamin A chromophore is usually 11 *cis* retinaldehyde (A1) which, when absorbs a photon of light, converts to all *trans*-stage by photoisomerization. This conformational change of the chromophore induces interaction with transducin (G protein), triggering the photoinduction cascade and change in receptor membrane potential [87]. All the photopigments have a characteristic absorption spectrum with a specific maximal sensitivity (λ_{max}). Vertebrate classes have been shown to have about 15 gene families of opsins to date [86].

In context to the involvement of opsins in neuroendocrine control of gonadal cycle in birds, three opsin classes have been the topic of extensive discussion owing to their anatomical localization, function, and action spectrum in avian brain, viz., rhodopsin, neuropsin, and VA opsin. Along with this, melanopsin has also been extensively studied, but its role in the circadian organization has been realized more than in photoendocrine pathway of reproduction. A few recent papers on drake also suggest a similar role of melanopsin on the regulation of reproductive behavior [48, 91]. Figure 1 shows localizations of few important opsins found to be expressed (either protein or mRNA) in avian brain (for details, see [88]).

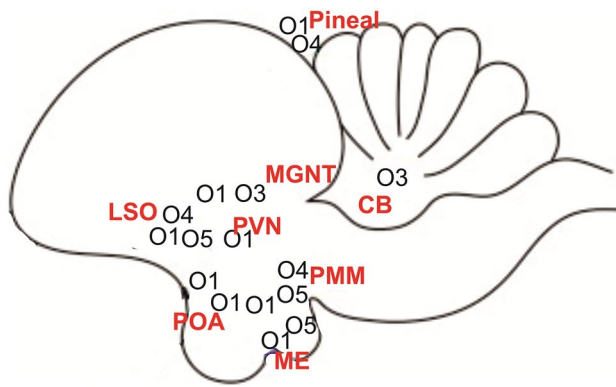


Fig. 1 Schematic diagram to demonstrate the distribution of different Opsins (either protein or mRNA) in an avian brain displayed on generalized sagittal section based on published Literature. O1: OPN1 (rhodopsin), O3: OPN3 (encephalopsin), O4: OPN4 (melanopsin), O5: OPN5 (neuropsin); CB, cerebellum; LSO, lateral septal organ; ME, median eminence; MGNT, medial geniculate nuclei thalamus; PMM, premammillary nucleus; POA, preoptic area; PVN, periventricular nucleus

2.2 Rhodopsin

Rhodopsins are photochemically reactive molecules with membrane embedded proteins, usually with seven alpha transmembrane helices as described above. Generally, these are classified into Type 1 (found in microbes like bacteria, archaea, fungi, and algae) and Type 2, which are the visual pigments in vertebrates and invertebrates. The photoreceptors in the quail brain were also found to be fitted to an action spectrum of rhodopsin with the maximum absorption at 492 nm [41]. To show the anatomical location of brain opsins, rhodopsin monoclonal antibody RET-P1 identified two cell populations of rhodopsin positive neurons: In lateral septum (SL) and in the infundibular nucleus (IN) and in median eminence in ring doves [104, 127]. It was also established in quail, mallard duck, and dark-eyed Juncos [96] and in house sparrows [129]. Seasonal and daily changes in rhodopsin expression have also been demonstrated using the RET-P1 antibody [48, 140]. The expression of rhodopsin mRNA has also been found to increase with increased duration of light and vary in different physiological states of migratory buntings with peak expression in the photo-stimulated state [67]. Rhodopsin has also been implicated as a brain photoreceptor in birds, fishes, and other lower vertebrates [68]. Along with the photoperiod-dependent expression, it has also been shown that rhodopsin expression has a circadian pattern, and light pulse in the night can elevate rhodopsin expression [61]. Thus, keeping in mind that light at the photoinducible phase, which usually falls in the early evening of many bird species induces gonadal development, rhodopsin may be proposed as the brain photoreceptor implicated in photoendocrine regulation of gonadal

development. Further, it has convincingly shown that rhodopsin (Rh1) in *Drosophila* along with light sensing also helps in temperature gradient discrimination [98]. Thus, it can also be postulated that rhodopsin may act to mediate temperature regulated control of neuroendocrine system in many vertebrates [30].

2.3 Neuropsin (OPN5)

Bioinformatic and molecular search for new opsins resulted in the isolation of a new opsin from mice and human tissues [116]. The gene shares only 20%-30% similarity with other opsin families and so has been assigned to a new family. It shows all the functionally important characteristics of other opsins but along with a lysine retinaldehyde chromophore-binding site in the seventh transmembrane domain [116]. Later, it was shown by analyzing purified OPN5 protein that it does not act as retinal photoisomerase but functions as UV-sensitive GPCR, which couples with Gi-type G protein [135]. Anatomically, it has been demonstrated that OPN5 is present in the human eye, brain, spinal cord, and testis [116]. OPN5 positive cells have been found in the chicken retina, pineal gland, and paraventricular organ (PVO). Further, it is described that three types of OPN5-like genes occur, out of which two are exclusively non-mammalian [117].

Detailed localization of OPN5 in quail brain revealed its presence in CSF contacting neurons in PVO region and in the external zone of ME, which contacts the pars tuberalis [77]. Functionally, it was also demonstrated alongside that OPN5 with the lambda max of 415 nm can induce voltage change in *Xenopus* oocyte when illuminated with light and thus inferred that OPN5 which is present in CSF contacting neurons can work as light sensors and produce membrane currents in the presence of light [77]. Another OPN5-like gene, OPN5L2 (OPN5-like 2) has been shown to be present laterally in the third ventricle and also in the adrenal gland, thus exhibiting the dual role of photosensing and chemosensing [80]. Localization of this OPN5L2 in vasotocin or GnRH-IR cells in the anterior hypothalamus reinforces its probable role as a deep brain photoreceptor. However, a direct test for the functional significance of OPN5 in seasonal neuroendocrine events revealed an inhibitory role of this opsin on *Tshβ*, which has a direct role in the photoperiodic gonadal induction. Injections of OPN RNAi into the ventricular system of border canaries caused an upregulation of *Tshβ* mRNA levels. The mRNA levels of neuropsin also did not change in response to light in the photoinducible phase [110]. Similar observations were made in photoperiodic red headed buntings where neuropsin levels did not vary in different lengths of photoperiod, and a significantly negative correlation was found between *Tshβ* and Neuropsin expression. Further, neuropsin was found to be highest in the photosensitive phase rather than the photo-induced

phase of the buntings [66]. Thus, the anatomical localization and functional considerations demonstrate a definite role of OPN5 in the photoperiodic regulated neuroendocrine system in birds, but the course of action on the mechanism is debatable.

2.4 VAopsin

Vertebrate Ancient opsin (VAopsin) was first isolated from cDNA pool of salmon ocular tissue with the derived amino acid sequencing showing about 37%–42% similarity with other opsin families and thus placed as a different opsin family [108] with amino acid identity revealing its presence before tetraploidy, thus its name. Structurally, the protein has many similar features as of other opsins with seven transmembrane domains and two conserved residues that are responsible for chromophore stabilization along with other features. However, on the third cytoplasmic domain, four nonconserved substitutions with two amino acid deletions make it unique as photoreception. Additionally, it does not have N-linked glycosylation sites, which are implicated in signal transduction. Thus, VAopsin is a small-sized opsin with light-dependent phosphorylation properties [108].

In birds, VAopsin is being reported in chickens with two isoforms: 972 bp VA and 1080 VAL, which encodes for a 323 and 359 amino acid long proteins, respectively. Both proteins have been shown to be capable of eliciting a retinal-dependent light response with current productions in patch clamp recordings [49]. VAopsin mRNA have been amplified from chicken hypothalamic cDNA and antibodies against it have shown positive signal in anterior hypothalamus adjacent to the third ventricle, supraoptic nucleus, PVN, and BnSTm. VAopsin lir-fibers were importantly noticed in ME adjacent to the PT [49]. In a different experiment, it was shown that both isoforms of VAopsin have an approximate lambda max of 490 nm, which corresponds to the previously accepted avian photoperiodic response peak at 492 nm [28]. In a recent study which attempted to functionally link both OPN5 and VAopsin with the seasonal control of reproductive axis in birds, Perez et al. [89] utilized intracerebroventricular infusion of adeno-associated viral vectors with shRNAi of OPN5 and VAopsin in seasonally breeding Japanese quails. Interestingly, it was found that long days induced significantly high levels of TSH β , hypothalamic gonadotrophin-releasing hormone-I (GnRH-I) mRNA, and paired testicular mass in VAopsin shRNAi-treated birds. In OPN5 shRNAi-treated quails, TSH β mRNA also increased but were not statistically different from the controls. Thus, contrary to the general understanding, the suppression of deep brain photoreceptors enhanced the reproductive axis' response to photostimulation rather than inhibiting it.

Finally, to the best of our knowledge, no further reports of VAopsin have been provided for any other song bird

species. Repeated attempts of cloning VAopsin from retinal and hypothalamic cDNA from photoperiodic redheaded buntings have also failed [67]. Thus, although convincing evidence shows the presence of VAopsin protein in chicken hypothalamus, its presence in other birds and its functional significance is still not explained.

2.5 The iodothyronine deiodinases

Decades of research have shown the involvement of thyroid hormone in governing seasonal reproduction but with different and often contradictory results. Thyroidectomy has been shown to either effect or not effect on gonadal development. In general, it has been convincingly shown that in birds, thyroxin treatment mimics the physiological effects of long days [132], and chronic thyroidectomy makes starlings [6] and sparrows [29] irresponsive to increase or decrease of photoperiod. Again, in both the species, the prevention of the onset of photorefractoriness by thyroidectomy resulted in high hypothalamic GnRH-I content as that of photosensitive birds, thus implying that the thyroid hormones can directly act on the central nervous system [29, 94]. It has also been demonstrated that thyroid hormone ICV (intracerebroventricular) injections can restore the effects of thyroidectomy in tree sparrows [133]. Search for molecular components in the MBH yielded two deiodinase enzymes, type 2 (Dio2) and type3 (Dio3), which formed the basis of thyroid hormones mediated effects in avian neuroendocrinology. Dio2 was found to be upregulated by a long photoperiod in the basal tuberal hypothalamus (BTH) [139]. Further analysis found a high concentration of active 3,5,3'-triiodothyronine (T3) and prohormone thyroxine (T4) in MBH tissue in response to long days from short days, although no change was detected in plasma concentration of these hormones [139]. Expression of thyroid hormone receptor genes of Thra, Thrb, Rxra, and Rxrg was also found to be localized in BTH, thus supporting the action site and role of thyroid hormones in avian hypothalamus. In another study, it was demonstrated that while Dio3 expression increases in response to long days, the reciprocal expression of Dio3 occurs in the mediobasal hypothalamus. This switching of expression preceded the rise of LH (luteinizing hormone) in plasma [137]. Structurally Dio2 is an outer ring selenodeiodinase that primarily catalyze the changes of T4 to T3 and rT3 to 3, 3'T2 [12]. Human Dio2 protein has a hydrophobic NH2 terminal, and this catalytic center is believed to be 100% conserved between rat, frog, and chicken [12]. It is responsible for producing more than 75% of active nuclear T3 in rat cerebral cortex [25]. Along with gonads, pituitary, brown adipose tissue muscles, coronary arteries, Dio2 expression has been found to be robust in tancytes lining the third ventricle [46]. On the other hand, Dio3, which was discovered earlier to Dio2, has the major share of inner ring deiodination activity

which causes inactivation of T3 and T4. It catalyzes the conversion of T4 to rT3 and T3 to 3, 3' T2, both of which are inactive forms. Thus Dio3 is responsible for preventing the thyroid hormone from gaining access to specific tissues at appropriate times [12].

The relative activity of these two enzymes, Dio2 and Dio3 (which have interestingly the same Km value for their substrate), finally regulates the intracellular concentrations of T3. It has been shown that the expression of both these enzymes is regulated in tissue specific temporal-spatial manner, thus producing varying levels of T3 at individual tissues [4]. The role of these enzymes has also been shown in both complete and partial photorefractoriness [130].

2.6 The upstream activators: Tsh β and Eya3

Increase in T3 level in hypothalamus just before rise in LH level in the first day of photostimulation in Japanese quail and the expression of thyroid deiodinase enzymes hinted a causal link between thyroid hormone, photoperiod, and gonadal regulation. Thus, search for the mechanism link between photoperiod and the deiodinase enzymes using the first day release model and genome wide microarray analysis yielded more upstream molecules and operation mechanisms in the quail hypothalamus. Expression analysis of mRNA collected at every 2 h of a single exposure of light at the photoinducible phase showed two major waves of gene expression trends one with Dio2, Dio3, ICER (inducible cAMP early repressor), etc. at 18 h and importantly two genes preceding this wave consisting of the β subunit of thyrotropin-stimulating hormone (*Tsh β*) and *Drosophila* homolog of Eyes absent type 3 (*Eya3*) at 14 h [78].

Localization of the TSH receptor in MBH further reinforced the potential role of thyroid hormones. In quail, it was found that the *Tsh α* subunit (CGA) mRNA, which together with *Tsh β* forms the functional TSH, was expressed rhythmically in the pars tuberalis. The causal relationship was established by the ICV injections of bovine TSH, which induced expression of Dio2 in a dose-dependent manner in the ventrolateral ependymal layer [78]. In birds, induction of *Tsh β* mRNA was subsequently shown in turkey [56], border canaries [110], and in migratory red headed buntings [65]. However, TSH β peptide was found to be localized in multiple brain regions [65] including septal region (SL) in response to long days, supseptal region (SSO), ependymal layer, infundibular nucleus (IN), inferior hypothalamus (IH), PT, and in pars distalis (PD) which supports previous findings [52]. Since TSH β expression was found in PD in both short-day and long-day exposed birds but only in PT in response to long days, it was suggested that the retrograde transport of TSH β occurs specifically from PT to MBH and not PD [65]. The TSH β -based induction of neuroendocrine system as further verified in melatonin proficient

mice demonstrating that TSH β gets induced in mouse PT with high expression attained in 5 long days owing to the circadian entrainment of PT circadian clock which brings the photoinducible phase in sync with the external photoconditions [69].

Search for the upstream activators of TSH β by late-night light exposure of mice revealed *Eya3* as an upstream gene candidate who can induce *Tsh β* expression with its partner Six1 through binding to *Tsh β* promoter [69]. *Eya3* (Eyes absent 3) is a member of EYA gene family first identified in *Drosophila* as a transcription factor in eye development and have two distinct domains: C terminal domain which interacts with other proteins and a tyrosine rich N terminal domain which contributes to its transactivational activity uniquely, *Eya3* has a dual function of transcription factor and has an intrinsic phosphatase activity [93]. Although the role of *Eya3* has been extensively studied in tissue development, recent advances also showed its involvement in photoperiodic effects. *Eya3* was identified as an upstream expressing gene in response to long photoperiod along with *Tsh β* in quail hypothalamus, but the mRNA expression site was found to be not correlated to the expression site of downstream genes like Dio2 and thus was discussed as not important in the transduction of photoperiodic information in birds [78]. *Eya3* mRNA expression sites include muscles, retina, and in pars tuberalis in MBH of both birds and mammals [26, 78]. Recently it was also shown that *Eya3* peptide expresses and is long day induced in ME, PT, SL, SM, PVN, IN, and IH but not in PD of pituitary [65]. With three E box elements in promoter (making it sensitive to Clock and Bmal1) and a single D box element (which makes it sensitive to Tef/Six elements), it provides support to the external coincidence model [26]. Accordingly, it may be assumed that *Eya3* helps in the transduction of photoperiodic information. In birds, as it is believed that melatonin does not play any role in photoperiodic-related events, *Eya3* has been suggested to be a part of the transduction of photoperiodic information pathway rather than directly involved in induction [65]. Expression of *Eya3* peptide in corresponding areas where rhodopsin is expressed in the hypothalamus [65, 104, 129] along with the evidence that *Eya3* mRNA expression correlates with the rhodopsin mRNA expression in response to increasing photoperiods [67] suggests that *Eya3* is involved in phototransduction in avian neuroendocrinology.

2.7 GnRH and GnIH: the downstream regulators of gonadal cycle

GnRH or Gonadotropin stimulating hormone was first isolated from the pig [70] and sheep [16]. Since then, it has been identified in most of the vertebrates from agnatha to humans [99]. GnRH is a decapeptide which has been shown to stimulate gonadotropin secretion. Three types of GnRH,

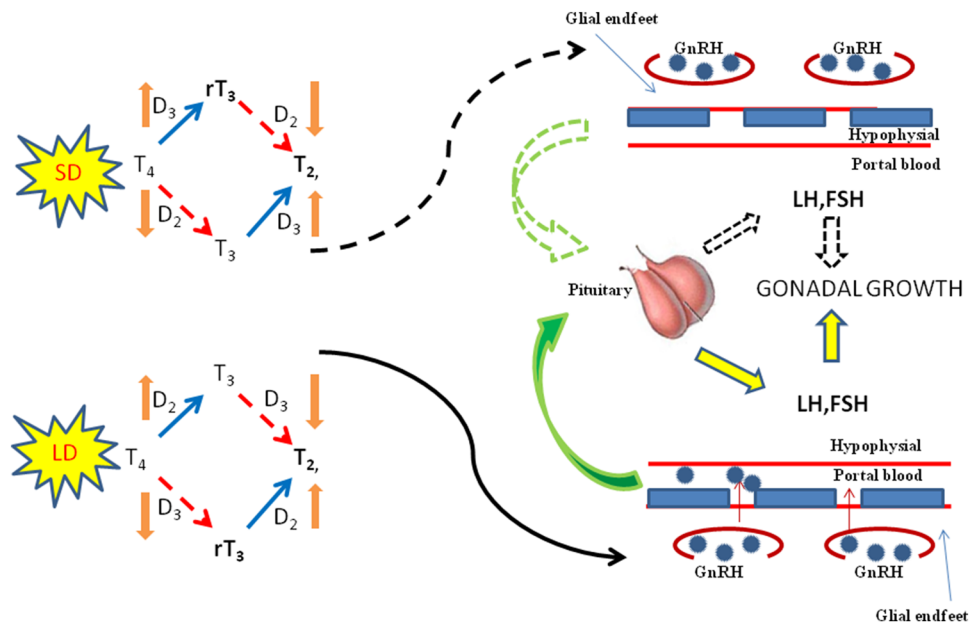
along with two types of GnRH receptors, have been reported to date in the avian brain [112]. GnRH-I [57] and GnRH-II [76] were first isolated from domestic chicken, while GnRH-III was isolated from lamprey and later found in song birds [7]. Anatomical localization of GnRH-I includes preoptic area with the fibers extending up to median eminence along the third ventricle and in the lateral septal area [75]. GnRH-II is distributed in the midbrain [75] and GnRH-III in the central nervous system, including the hippocampus and song control regions in song birds [7]. It has been suggested that all three types of peptide have the ability to induce secretion of LH but in different capacities [92]. However, GnRH-I plays a major role in the release of LH [97]. Of more importance is the seasonal plasticity inactivity of GnRH-I-associated neurons in septo-preoptic infundibular regions in the avian brain, which has overwhelmingly accepted as the central control of seasonal breeding physiologies [2]. High content of GnRH-I has been detected in stimulated and breeding conditions with the inhibition of its secretion being associated with the termination of breeding activity and the onset of photorefractoriness. Birds regain their photosensitive physiologies with the increase in GnRH-I content in POA (preoptic area) [31]. Further, in starlings, it has been demonstrated that GnRH immunoreactivity and perikarya seem the same in photosensitive and photostimulated birds, but in ME, the staining was much higher in stimulated birds suggesting the difference between GnRH production or storage and its transport or release [42]. Activation of GnRH neurons occurs as soon, as the first long day as demonstrated in white-crowned sparrows [95], and red headed buntings [65]. In addition, in chicken, GnRH-II receptor, cGnRH-IIIR increases in photostimulated birds, indicating an important role of GnRH-II in the neuroendocrine control of avian reproduction [101]. Photoperiod acts as the main regulator of the GnRH activity, although food, social conditions, temperature, and the presence of conspecific has also been shown to affect GnRH production and release. Overall, the environmental factors activate the GnRH, which in turn helps in the release of gonadotropin in the portal system. Further, gonadotropin increases the production of sex steroids which again produces negative feedback on GnRH system [58]. Testosterone, estrogens, along with hypothalamic vasointestinal peptide (VIP) has been shown to inhibit GnRH expression [34]. Another dodecapeptide, the Gonadotropin-inhibitory peptide (GnIH) has been shown to influence the GnRH expression in a negative way, with its expression being inversely related to GnRH expression in quail [118]. The presence of GnIH has been demonstrated in many avian species in the last decade, regulating the release and synthesis of GnRH through GnIH receptors [119]. Structurally, GnIH is a hypothalamic neuropeptide with a C terminal RFamide motif with a dodecapeptide structure. In birds, GnIH has been localized in the paraventricular

region (PVN) in the hypothalamus with projection up to the ME (median eminence) [118]. Functionally, it has been shown that intravenous injections of GnIH can reduce the levels of blood LH in stimulated white crown sparrows and also stop the GnRH induced LH in non-stimulated birds [84]. Further, synthesis of LH β and FSH β is inhibited by GnIH both in vitro and in vivo [22]. GnIH receptor (GnIH-R) has been found to be co-localized with LH β and FSH β mRNA containing cells, thus showing a direct link between these gonadotropins and GnIH [64]. But of interest, more is the conserved mechanism of GnIH:GnRH interactions in birds. GnRH neurons have been found to be in contact with GnIH neurons in most of the bird species studied [8]. Along with effect on GnRH and gonadotropins, GnIH influences many other behaviors like feeding and singing in song birds [121]. Photoperiod and melatonin have been shown to directly control the release and synthesis of GnIH, which being negatively correlated with LH levels [21]. Interestingly, GnIH also exhibits interaction with melatonin, the master hormone. Low expression of GnIH is associated with pinealectomy along with enucleation (thus removing major sources of melatonin). Further, high GnIH under short days (SD) also is associated with high melatonin in SD [120]. The presence of Melatonin receptor Mel1c on GnIH neurons further demonstrated a direct effect of melatonin on GnIH. Overall, GnRH and GnIH system underlies the photoperiod responsive neuroendocrine mechanism, which ultimately controls the avian reproduction (Fig. 2).

3 The mechanism of photoneuroendocrine control of the gonadal cycle

Recent research both in mammals and birds hints that the photoneuroendocrine control of gonadal induction is much conserved in both birds and mammals except for the perception/input mechanisms of light information. Photoperiod in mammals is perceived by the retina, which then regulates the duration and peak of melatonin, finally laying the foundation of photoendocrine control of reproduction. Birds perceive the photoperiodic information directly in the brain in all probability in MBH, where the presence of various photoreceptor molecules has been shown. Evidence suggests that rhodopsin may affect the deep brain photoreceptor, which plays a dominant role in birds for perceiving light information [66] with neuropsin (OPN5) exerting an inhibitory effect on the induction process [67, 110]. In mammals, melatonin acts to control the expression of *Eya3* by acting on its promoter, which has a Tef-binding element. *Eya3* acts as a coactivator for Six1, which together binds to the SO site on *Tsh β* promoter. Tef elements also bind to the D box of *Tsh β* promoter, and together, these activate the *Tsh β* expression [26]. In birds, however, a similar mechanistic

Fig. 2 Schematic diagram showing the effect of photoperiods (short day; SD and long day; LD) on induction of Dio2/Dio3 which in turn regulates the levels of active thyroid (T3) or inactive thyroid (rT3). This in turn regulates the release of GnRH by glial endfeets to the hypophysial portal system. The GnRH then induces the release of LH, FSH by the pituitary ultimately resulting in gonadal regulation



approach of proving *Eya3* as a *Tshb* activator has still not been undertaken even though *Eya3* expression is closely linked with *Tshb* expression [78]. However, expression of *Eya3* and *Tshb* in response to different increasing durations of a single photoperiod shows a significant correlation with each other [66]. Also, it has been suggested that *Eya3* can induce *Tshb* in PT, since *Eya3* protein expression increases significantly in ME and *Tshb* peptide expression in PT in response to long days but still colocalization of both peptides was not recorded [65]. The induction of *Tshb* (either by *Eya3* or other mechanisms) results in the induction of *Dio2* mRNA in the hypothalamus (Birds: [78], mammals: [137]). *Dio2*, in turn, increases the local concentration of active T3. Since, the induction of *Dio2* occurs in the ependymal cells of basal tuberal hypothalamus (ME and IN), it has been suggested that the local increase in active T3 in the ME (Fig. 2) may be responsible for the morphological changes in GnRH nerve terminals ultimately resulting in the release of GnRH from ME to pituitary [134]. This GnRH binds to specific and high affinity GnRH receptors in the pituitary gonadotrophs triggering a series of calcium-dependent signaling pathways from phospholipase C to protein kinase C ultimately resulting in exocytosis of LH and follicle-stimulating hormone (FSH). The secretion pattern of LH and FSH differs in certain conditions, which may suggest a differential control by GnRH on these glycoprotein gonadotropins [1].

In contrast to the indispensable role of thyroid hormones in the neuroendocrine regulation of gonadal cycle, some species of birds like quails show the gonadal development even after the removal of the thyroid gland. Subtractive hybridization techniques revealed another thyroid independent pathway of GnRH induction mediated by $TGF\alpha$. $TGF\alpha$ was also found to have a photoperiod-dependent expression with high

expression in long days [115]. Comparison on German and Swedish populations of great tits revealed that although LH and FSH secretion occurs in response to long days, reciprocal switching of *Dio2*-*Dio3* occurs only in one population showing the difference in temporal pattern with other reproductively associated gene expressions. This supported that GnRH control may occur independently of thyroid responsive genes in different species of birds [90]. Another study in European starlings demonstrated no correlation of *Dio2* expression with seasonal gonadal volume, which was otherwise highly correlated to GnRH expression [9]. Thus, the neuroendocrine control of seasonal gonadal cycle may be more complex than previously anticipated and may involve other important pathways which contributes to the complexity and redundancy of the system in birds. Understanding of this photoperiodic mechanism to date in mammals and in birds has been summarized in Fig. 3.

4 Non-reproductive outputs of photoperiodism in birds

Effects of long and short photoperiodic cycles have been investigated in a lot of other phenomena like molt, migration, fat deposition, etc. Long days have a relatively direct effect on prenuptial molt, vernal migration, vernal fat deposition, vernal hyperphagia, and gonadal growth and indirectly on development of photorefractoriness, postnuptial molt, autumnal fat deposition, and migration [39]. Whereas, the short day terminates refractoriness and helps in the restoration of the photoperiodic response mechanism. Behavioral studies also demonstrated that long day induces nest building activities in doves, and pinealectomy abolishes it [71].

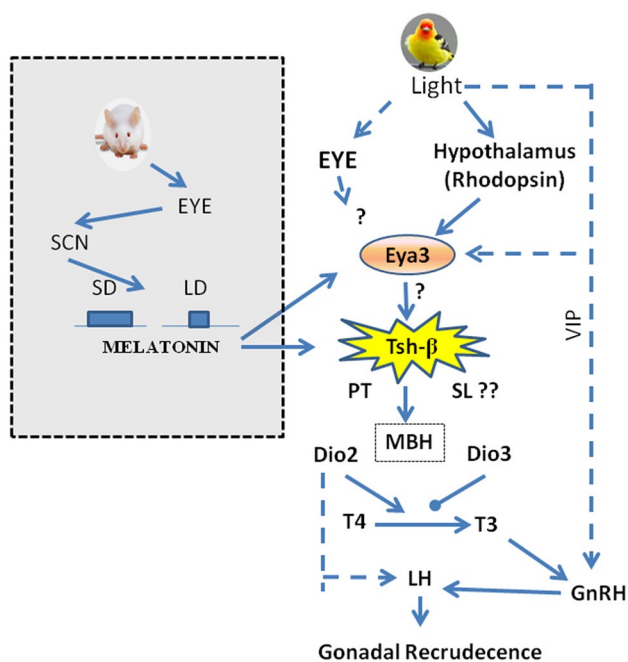


Fig. 3 Diagrammatic representation of the current status of knowledge on molecular regulation of photoperiod-induced seasonal reproductive physiology of both mammals and birds. The broken lines and question marks represent the gap of knowledge. The arrows with blunt ends represent negative impact on the phenomenon

Parental feeding behavior has also been shown to be prolactin induced and gets abolished by preoptic area lesioning in ring dove [106]. This may lead to a conclusion that long days have stimulatory effects on many such reproduction-associated activities.

Several studies have reported a significant effect of photoperiod, independent of hormones, on avian seasonal brain plasticity and thus hinting at a more direct pathway between light/photoperiodic stimulation and NP. A hormone (mainly testosterone) independent effect on the growth of song nuclei has been reported in many avian species, e.g., dark-eyed juncos [33], European starlings [10], gambel's white-crowned sparrow [107], tree sparrow [11], and blue tits [18]. In addition to these seasonal changes in hippocampal size (relating to spatial behavior and memory) and seed storing behavior has also been shown to be influenced by photoperiodism [136]. Recent advancements in MRI technology, such as diffusion tensor imaging, have expanded our comprehension of the massive neuroplasticity underlying seasonal song learning in avian brains [83]. In addition to confirming many of the known seasonal and testosterone-induced changes in neuroplasticity within the SCS of the same bird, the discovery and application of *in vivo* MRI techniques in songbirds have yielded a number of novel and intriguing results. During the photosensitive phase, it has been demonstrated that starlings endure multimodal neuroplasticity, which includes

structural and functional changes in sensory systems, such as the visual, auditory, and even olfactory systems. This evidence of plasticity in photosensitive phase where almost all 'reproductive/seasonal' hormone levels are very low or absent suggests that light/photoperiod may be involved in direct induction of neuroplasticity [83]. Of direct interest in context to the current review, in seasonally reproducing birds like starlings, along with the song, olfactory and auditory system plasticity, a significantly high plasticity was seen in preoptic area and ventromedial hypothalamic nuclei, which lies dorsally very close to optic chiasm [32]. Both of these areas also receive retinal inputs. Further, naturally occurring seasonal plasticity has been observed at the level of the visual Wulst (homologue of the visual cortex) showing significant increase in dendritic thickness and spine density in the breeding season, related to active state and increased sensitiveness of these neurons in songbirds [109]. Therefore, speculations may be made that avian eye/retina may have some role to play in mediating seasonal neuroplasticity in avian brains.

5 Avian eyes and its pathways

The visual capabilities of birds are comparable to, and in some instances superior to, those of another visually dependent group of vertebrates, the primates. Unique specializations of avian visual systems (as compared to primates) include the existence of double cones, distinct photopigment absorption spectra, the presence of oil droplets, centrifugal efferents to the retina, and an emphasis on the collothamic (tectofugal) visual pathway. Multiple sources of evidence indicate that the avian visual system was primarily driven by modifications to the reptilian basic plan in support of flight behaviors. The development of the collothamic pathways encouraged the development of the avian telencephalon as the site for more complex social and feeding behaviors [103, 128].

Two major visual pathways connect the retina to the telencephalon in all amniotes: the collothamic (or tectofugal) and the lemnothalamic (or thalamofugal) pathways. In birds, the connection patterns of the two pathways are comparable to those of mammals, despite the vastly different functional functions. The collothamic pathway in birds connects the retina to the optic tectum, the thalamic nucleus rotundus (nRt), and the ectostriatum in the dorsal ventral ridge [17]. This pathway resembles the primate collothamic pathway in that both pathways process visual information from the optic tectum/superior colliculus, which is one of the brain's most phylogenetically ancient structures [17, 102]. The avian nRt is compared to the primate pulvinar as the primary thalamic target of the tectal efferents, whereas the avian ectostriatum is compared to a portion of

the extrastriate cortices as the telencephalic target of the collothalamal pathway.

The avian lemnothalamic pathway extends from the retina to the dorsal thalamic nuclei (called the principal optic nuclei of the thalamus, OPT) to the visual wulst region of the telencephalon [17, 102]. The OPT and the visual wulst are, respectively, compared to the mammalian LGd and striate cortex in that they are the thalamic targets of the direct retinal input and the telencephalic targets of the thalamic nuclei. The degree of development of the two pathways is another distinction between mammalian and non-mammalian retinal projections. The mammalian—particularly primate—lemnothalamic pathway is significantly more developed and differentiated than the collothalamal pathway. The primate LGd, for example, is highly segregated based on cytoarchitecture, function (magnocellular and parvocellular layers), and connections (ipsi- and contra-lateral retinal input). In contrast, in many sauropsids (birds and reptiles), the lemnothalamic pathway is relatively underdeveloped and undifferentiated compared to the collothalamal pathway, which comprises the optic tectum, the most important visual center in nonmammals [17, 102].

On a different note, there are two systems for detecting light in animals (mostly known from mammalian studies): (i) The classical visual system for image formation (IF) (ii) The non-image-forming (NIF) visual circuit. The NIF has been recently described in mammals (For details, see [44] and it modulates many physiological, behavioral, and cognitive responses which are not associated with image perception. These responses include timing of circadian rhythms, heart rate, body temperature, the sleep–wake cycle, performance, cognitive brain responses, etc. [44]. This NIF circuit starts from intrinsically photoreceptive retinal ganglionic cells (ipRGCs) which contains opsin protein called Melanopsin (OPN4, also mentioned above). Melanopsin is a non-visual photopigment maximally sensitive to blue light (460–480 nm of the spectrum) [62]. The primary targets of ipRGCs include VLPO and the ventral subparaventricular zone (controlling sleep induction and general activity levels). In addition, ipRGCs innervate limbic regions like lateral habenula and the medial amygdala thus showing the direct role of light in the regulation of mood and cognitive functions [62]. In birds, although melanopsin expression has been shown in many brain regions and in retina, no NIF pathway has been elucidated still and hence presents for an exciting new field for research.

6 Role of eyes in photoperiodism

In birds, the anatomical neuronal substrate for gonadotropin synthesis and release is directly influenced by the neural system, which perceives the changes in the length of the day

with hypothalamus being the most highlighted one. Following the *Nomina Anatomica Avium* [15], the hypothalamus of birds can be divided into three main portions—the preoptic region, the medial (tuberal) region, and the caudal (mammillary) region. Owing to extensive species diversity for brain morphology and functionally distinct cell types, a comprehensive understanding of the avian hypothalamus becomes difficult with functional studies and anatomical descriptions, often having a variance with each other. In terms of circadian clock regulation of physiology, birds have the capacity to perceive information about the photic environment by the retina, pineal gland, as well as by deep encephalic photoreceptors [104]. Depending on the species, circadian pacemaking at the whole-organism level is organized by autonomous and anatomically distinct oscillators localized in the retina, the pineal gland, and the hypothalamus. Several lines of evidence suggest that these components interact with each other to produce stable circadian rhythmicity of the animal (for details, see [113]). In Japanese quail, complete deafferentation (i.e., isolation from afferent neuronal input) of the tuberal hypothalamus (or infundibular nucleus, IN) results in blocking testicular growth with a rapidly lowering of LH levels [27]. More specific differentiation in the anterior hypothalamus in quail suggests that the preoptic region and an area immediately posterior to this region are necessary for the testicular photoperiodic response, which is consistent with the similar lesion studies in female quail (photoperiodic response of egg laying), the male duck [5], and pigeons [14]. Taken together, these results suggest the following: (1) MBH is not exclusively the site for photoperiodic response, although it does have the primary role in the control of photoperiodic GnRH release. (2) Fibers from the anterior hypothalamus, especially the preoptic region to the tuberal hypothalamus of the MBH, are important for PTM. (3) The "carry-over" effect of one long-day-induced LH surge is not totally controlled by the MBH.

6.1 Retinal projection and the retinohypothalamic transmission

Attempts have been made to locate the hypothalamic oscillator in various avian species using tract-tracing techniques, taking into account the importance of retinohypothalamic transmission of photic information to the suprachiasmatic nuclei (SCN) in mammalian hypothalamic pacemaker entrainment. However, the retinal input to the SCN in the pigeon has not been found [24], but later dense arborizations of retinal fibers were observed in the SCN of the same species [100]. Similar inconsistent finding was found in the birds of house sparrow, quail, and starling, where either retinal input was observed [51], or no retinal fibers were identified in the SCN [20]. A large number of retinal projections were consistently found in the ventral portion of the lateral

hypothalamic nucleus (LHN) in all species investigated, but for this retinal projection, no systematic nomenclature has been used [20, 51].

The first study to visualize ganglionic cell projection to hypothalamus showed that HRP injection in the preoptic-anterior hypothalamic formations leads to retrograde transport of the enzyme to some ganglion cells in the retina, whereas only rare labeled neurons could be detected in the anterior-basal hypothalamus [82]. Autoradiographic studies demonstrated that tritiated leucine or proline was incorporated into retinal cells and transported along their axons to the anterior hypothalamus of pigeons and jackdaws. Further, as electrolytic lesions in preoptic-anterior hypothalamic region blocked the photo-induced testes growth, plasma LH increase, and testosterone-level augmentation, it was derived that function of such retinal–hypothalamic connections might be to participate in the photosexual reflex [73].

Electron and light microscopic studies on the retinohypothalamic pathway in duck after unilateral optic nerve transection showed some very fine degenerating fibers in the anterior hypothalamus, proving that a circumscribed region of the anterior hypothalamus of the duck (SCN) receives direct retinal inputs. These degenerating fibers within the anterior hypothalamus displayed degenerating fibers and axonal arborizations, along with degenerating presynaptic profiles and postsynaptic membranes [13]. The precise projection of retinal fibers showed that the nucleus with degenerating fibers was bordered on its lateral side by the lateral part of the supraoptic nucleus, on its medial rostral side by the medial part of the supraoptic nucleus, and medial caudal side by the preoptic recess and the paraventricular nucleus [13]. Similar findings were reported in pigeons [51]. Besides the direct connections, visual connectivity can also be traced to septal areas and many other areas of the brain indirectly. Studies have shown the connection from optic tectum to the septal region in pigeon and owl [19, 45] or through anterior hypothalamus. It is interesting to note that the connection of eye or retina with the preoptic area may be direct [82] or may be derived indirectly through the geniculate leaflet (Glv), as shown by Dil (dialkylcarbocyanine) tracing studies showing links between Glv and preoptic area in quail [3].

7 Evidence: for and against

As discussed above, based on a large number of studies in diverse groups of birds and other lower vertebrates, it is now generally accepted that eyes/retina have no role to play in the regulation of seasonal reproductive physiology of at least birds owing to the presence of deep brain photoreceptors [40]. To summarize, gonadal growth could still be stimulated by light even after the optic nerves were cut in domestic ducks and by shining light directly onto

various brain regions in enucleated ducks [13]. No difference could be found in the testicular response of blind and normal sparrows (*Passer domesticus*) subjected to a variety of experimental light regimes, but the response was abolished by injecting India ink beneath the skin of the head [74]. In quails, radioluminous paint in various areas of the brain facilitated gonadal growth but had no effect if painted in the eyes [53]. The existence of extraretinal photoreceptor was later confirmed in other avian species including house sparrow, *Passer domesticus* [74], chicken, *Gallus domesticus* [55]; white-crowned sparrow, *Zonotrichia leucophrys* and golden-crowned sparrow, *Zonotrichia atricapilla* [47]; Japanese quail, *Coturnix coturnix japonica* [53] and American tree sparrow, *Spizella arborea* [131], as well as in fish [114], amphibians [123], and reptiles [124]. In recent years, these photoreceptors have been classified as rhodopsin [104], neuropeptide [77], VAopsin [49], or melanopsin [91] as detailed above in this review.

In contrast, a few studies examined if the eyes have any role to play in the regulation of photoperiodic seasonal physiology. Based on two studies done simultaneously at the University of Tokyo and the University of California (Davis) on quails, they reported that mature enucleated quail is resistant to lighting conditions that are inhibitory to the gonads and enucleated birds did not stop laying eggs even after being exposed to short days [54]. It was also found that after attaining sexual maturity, even in alternating short and long days, enucleated male quails maintained an active cloacal gland regardless of the photoperiod exposure, which indicates a functional endocrine testes status [54] (Fig. 4A). A similar absence of gonadal regression on exposure to short days was confirmed in enucleated quails [79]. Further, complete differentiation of the infundibular complex in quails resulted in similar resistance to gonadal regression upon short-day exposure just like the enucleated birds, supporting the idea that retina may indeed be transmitting inhibitory signals to hypothalamic areas [79]. Similar inhibition of cloacal gland regression (Fig. 4A) was also reported for enucleated quails exposed to short photoperiods of incandescent light [105].

While testing the impact of retinal inputs on steroid sensitivity, it was observed that bilateral enucleation renders quails less sensitive to the gonadoinhibitory effects of testosterone propionate in birds under long photoperiod [60], suggesting that retinal inputs may alter the steroidal sensitivity of hypothalamus. Comparing the effects of unilateral and bilaterally enucleation on plasma LH levels, it was found that although blinding does not stop the rise of plasma LH levels or body weight upon photoperiodic stimulation, bilaterally enucleated birds had higher LH levels (Fig. 4B) indicating the removal of certain inhibitory signals originating from retina [138] as proposed by other reports described above. These effects on LH are confirmed by another study on enucleated quails where levels of LH are found to be

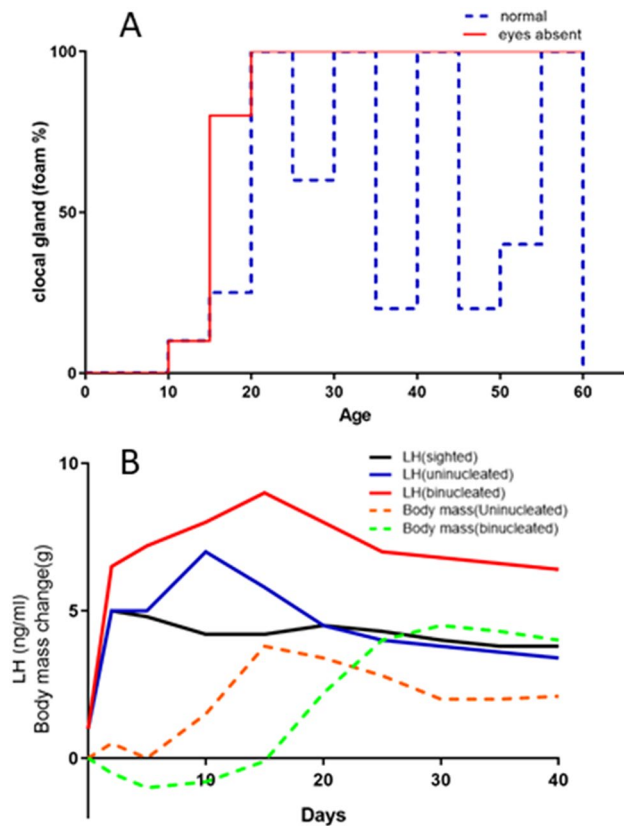


Fig. 4 Role of eyes in regulation of cloacal activity, LH levels in plasma and body weigh difference in quails. **A** The cloacal gland activity in enucleated and normal birds across development exposed to alternating photoperiod of short days and long days (adapted from [54]). **B** Luteinizing hormone (LH) levels in plasma and body mass difference in normal, unilateral enucleated, and bilaterally enucleated quails across days (adapted from [138])

higher that are exposed to long photoperiods than those of the short days (Fig. 4B). Thus, it was proposed that retina transmits short day signal, which has an inhibitory effect on LH production [59]. Testing the retina's influence on neuronal responses using spontaneous and flash evoked multiple units discharges neuronal recordings in tuberal and dorsal infundibular region of quails, which showed that complete blinding suppresses the flash evoked multiple unit activity (MUA) in the tuberal region though the MUA persisted in spontaneous light induction [81]. This implies that hypothalamic firing rates were dependent upon nervous messages originating from the retina.

More than a decade later, the role of eyes on photoperiodic regulation of gonadal cycle was again tested, showing that pinealectomy in combination with enucleation significantly decreases the expression of GnIH mRNA and peptide levels in paraventricular nuclei and median eminence of quails [120]. This is in accordance with the findings that eyes exert an inhibitory role on photostimulation as GnIH is also an inhibitory gonadotropin. All these findings hint

toward the proposition that eyes/retina can differentiate between photoperiodic changes and relay some kind of yet uncharacterized signal to the brain to modulate the photoperiod-induced responses, though these responses are independent of the retina and in most probability are a functional consequence of deep brain photoreception. Indeed, we recently showed that birds' eyes/retina could indeed differentiate between long and short photoperiod with significantly high expression of both mRNA and protein of EYA3 and TSH-beta upon exposure to long photoperiods [66].

8 Conclusions and perspective

Seasonal variation in the photoperiod is the most appropriate cue for a seasonal bird to plan its reproductive physiology of gonadal recrudescence and regression. It has been well established that birds and other non-mammalian vertebrates use the extraocular photoreceptors which may be present in MBH or associated regions to measure the photoperiodic time. The eyes are not essential for photoperiod-induced testicular growth. Long-day lengths continue to induce testes development even after total severance of the optic nerves or removal of both eyes in a variety of bird's species, but critical analysis of the available literature to date suggests an interesting role which the eyes play in the regulation of the seasonal reproductive cycle of avian taxa. It may be highly interesting to clarify the molecular mechanism on how the retina sends inhibitory signals or regulate the expression of GnIH to ultimately influence the gonadal physiology. Multiple peptides are known to originate in retina and travel to brain like OTX2 [111] and PACAP [50]. Indeed, PACAP has also been shown to interact with melanopsin and regulate neuronal responses related to the circadian clock [63]. Finally, as retina expresses primary molecules of photoperiodic cascade like EYA3, TSH-beta along with Dio2 and Dio3, it can serve as an important tissue to study the interaction of opsins and photoperiodic molecules which still is elusive.

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Declarations

Conflict of interest All the authors declare no conflict of interest.

References

- Anderson, L. (1996). Intracellular mechanisms triggering gonadotrophin secretion. *Reviews of Reproduction*, *1*, 193–202.
- Ball GF and Hahn, TP 1997 GnRH neuronal systems in birds and their relation to the control of seasonal reproduction; in *Proceedings of the GnRH Neurons: Gene to Behavior* (eds) IS Parhar and Y Sakuma (Shuppan Publishers: Tokyo, Japan) pp 325–342
- Balthazart, J., Dupiereux, V., Aste, N., Vigliettipanzica, C., Barrese, M., & Panzica, G. C. (1994). Afferent and efferent connections of the sexually dimorphic medial preoptic nucleus of the male quail revealed by in-vitro transport of dii. *Cell and Tissue Research*, *276*, 455–475.
- Bates, J. M., St Germain, D. L., & Galton, V. A. (1999). Expression profiles of the three iodothyronine deiodinases, D1, D2, and D3, in the developing rat. *Endocrinology*, *140*, 844–851.
- Benoit, J., Assenmacher, I., & Brard, E. (1959). Action of prolonged permanent lighting on the testicular development of the Pekin duck. *Archives d'Anatomie Microscopique et de Morphologie Expérimentale*, *48*, 5–11.
- Bentley, G. E., Dawson, A., & Goldsmith, A. R. (2000). Lack of gonadotrophin-releasing hormone (GnRH) neuron response to decreasing photoperiod in thyroidectomized male starlings (*Sturnus vulgaris*). *Journal of Experimental Zoology*, *287*, 74–79.
- Bentley, G. E., Moore, I. T., Sower, S. A., & Wingfield, J. C. (2004). Evidence for a novel gonadotropin-releasing hormone in hypothalamic and forebrain areas in songbirds. *Brain, Behavior and Evolution*, *63*, 34–46.
- Bentley, G. E., Kriegsfeld, L. J., Osugi, T., Ukena, K., O'Brien, S., Perfito, N., Moore, I. T., Tsutsui, K., & Wingfield, J. C. (2006). Interactions of gonadotropin-releasing hormone (GnRH) and gonadotropin-inhibitory hormone (GnIH) in birds and mammals. *Journal of Experimental Zoology Part A: Comparative Experimental Biology*, *305*, 807–814.
- Bentley, G. E., Tucker, S., Chou, H., Hau, M., & Perfito, N. (2013). Testicular growth and regression are not correlated with Dio2 expression in a wild male songbird, *sturnus vulgaris*, exposed to natural changes in photoperiod. *Endocrinology*, *154*, 1813–1819.
- Bentley, G. E., Van't Hof, T. J., & Ball, G. F. (1999). Seasonal neuroplasticity in the songbird telencephalon: A role for melatonin. *Proceedings of the National academy of Sciences of the United States of America*, *96*, 4674–4679.
- Bernard, D. J., Wilson, F. E., & amd Ball GF. (1997). Testis-dependent and -independent effects of photoperiod on volumes of song control nuclei in American tree sparrows (*Spizella arborea*). *Brain Research*, *760*, 163–169.
- Bianco, A. C., Salvatore, D., Gereben, B., Berry, M. J., & Larsen, P. R. (2002). Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. *Endocrine Reviews*, *23*, 38–89.
- Bons, N. (1976). Retinohypothalamic pathway in the duck (*Anas platyrhynchos*). *Cell and Tissue Research*, *168*, 343–360.
- Bouille, C., & Bayle, J. D. (1973). Effects of hypothalamic stimulation on pituitary-adrenocortical activity in conscious unrestrained pigeons. *Neuroendocrinology*, *12*, 284–294.
- Breazile JE and Kuenzel WJ 1993 Systema nervosum centrale; in *Handbook of Avian Anatomy: Nomina Anatomica Avium* (eds) JJ Baumel, AS King, JE Breazile, HE Evans and JC Vanden Berge (Publication of Nuttal., Ornithology Club) pp 493–554.
- Burgus, R., Butcher, M., Amoss, M., Ling, N., Monahan, M., Rivier, J., Fellows, R., Blackwell, R., Vale, W., & Guillemin, R. (1972). Primary structure of the ovine hypothalamic luteinizing hormone-releasing factor (LRF) (LH-hypothalamus-LRF-gas chromatography-mass spectrometry-decapeptide-Edman degradation). *Proceedings of the National academy of Sciences of the United States of America*, *69*, 278–282.
- Butler, A. B., & Hodos, W. (1996). *Comparative Vertebrate Neuroanatomy: Evolution and Adaptation*. Wiley-Liss.
- Caro, S. P., Lambrechts, M. M., & Balthazart, J. (2005). Early seasonal development of brain song control nuclei in male blue tits. *Neuroscience Letters*, *386*, 139–144.
- Casini, G., Porciatti, V., Fontanesi, G., & Bagnoli, P. (1992). Wulst efferents in the little owl *Athene noctua*: An investigation of projections to the optic tectum. *Brain, Behavior and Evolution*, *39*, 101–115.
- Cassone, V. M., & Moore, R. Y. (1987). Retinohypothalamic projection and suprachiasmatic nucleus of the house sparrow, *Passer domesticus*. *The Journal of Comparative Neurology*, *266*, 171–182.
- Chowdhury, V. S., Yamamoto, K., Ubuka, T., Bentley, G. E., Hattori, A., & Tsutsui, K. (2010). Melatonin stimulates the release of gonadotropin-inhibitory hormone by the avian hypothalamus. *Endocrinology*, *151*, 271–280.
- Ciccone, N. A., Dunn, I. C., Boswell, T., Ubuka, T. K., & T, Ukena K and Sharp PJ. (2004). Gonadotropin inhibitory hormone depresses gonadotropin alpha and follicle-stimulating hormone beta subunit expression in the pituitary of the domestic chicken. *Journal of Neuroendocrinology*, *16*, 999–1006.
- Colwell, R. K. (1974). Predictability, Constancy, and Continuity of Periodic Phenomena. *Ecology*, *55*, 1148–1153.
- Cooper, M. L., Pickard, G. E., & Silver, R. (1983). Retinohypothalamic pathway in the dove demonstrated by anterograde HRP. *Brain Research Bulletin*, *10*, 715–718.
- Crantz, F. R., Silva, J. E., & Larsen, P. R. (1982). An analysis of the sources and quantity of 3,5,3'-triiodothyronine specifically bound to nuclear receptors in rat cerebral cortex and cerebellum. *Endocrinology*, *110*, 367–375.
- Dardente, H., Wyse, C. A., Birnie, M. J., Dupre, S. M., Loudon, A. S. I., Lincoln, G. A., & Hazlerigg, D. G. (2010). A Molecular Switch for Photoperiod Responsiveness in Mammals. *Current Biology*, *20*, 2193–2198.
- Davies, D. T., & Follett, B. K. (1975). The neuroendocrine control of gonadotrophin release in the Japanese quail. II. The role of the anterior hypothalamus. *Proc. R. Soc. Lond. B. Biol. Sci.*, *191*, 303–315.
- Davies, W. I., Turton, M., Peirson, S. N., Follett, B. K., Halford, S., Garcia-Fernandez, J. M., Sharp, P. J., Hankins, M. W., et al. (2012). Vertebrate ancient opsin photopigment spectra and the avian photoperiodic response. *Biology Letters*, *8*, 291–294.
- Dawson, A. (1998). Thyroidectomy of house sparrows (*Passer domesticus*) prevents photo-induced testicular growth but not the increased hypothalamic gonadotrophin-releasing hormone. *Gen. Com. Endocrinol.*, *110*, 196–200.
- Dawson, A. (2005). The effect of temperature on photoperiodically regulated gonadal maturation, regression and moult in starlings – potential consequences of climate change. *Functional Ecology*, *19*, 995–1000.
- Dawson, A., & Goldsmith, A. R. (1997). Changes in gonadotropin-releasing hormone (GnRH-I) in the pre-optic area and median eminence of starlings (*Sturnus vulgaris*) during the recovery of photosensitivity and during photostimulation. *Journal of Reproduction and Fertility*, *111*, 1–6.
- De Groof, G., Verhoye, M., Poirier, C., Leemans, A., Eens, M., Darras, V. M., & Van der Linden, A. (2009). Structural changes

- between seasons in the songbird auditory forebrain. *Journal of Neuroscience*, 29(43), 13557–13565.
33. Deviche, P., & Gullledge, C. C. (2000). Vocal control region sizes of an adult female songbird change seasonally in the absence of detectable circulating testosterone concentrations. *Journal of Neurobiology*, 42, 202–211.
 34. Deviche, P., Saldanha, C. J., & Silver, R. (2000). Changes in brain gonadotropin-releasing hormone- and vasoactive intestinal polypeptide-like immunoreactivity accompanying reestablishment of photosensitivity in male dark-eyed juncos (*Junco hyemalis*). *General and Comparative Endocrinology*, 117, 8–19.
 35. Dixit, A. S., & Singh, N. S. (2011). Photoperiod as a proximate factor in control of seasonality in the subtropical male Tree Sparrow, *Passer montanus*. *Frontier Zoology*, 8, 1–12.
 36. Dixit, A. S., & Singh, N. S. (2020). Circadianversuscircannual rhythm in the photoperiodic programming of seasonal responses in Eurasian tree sparrow (*Passer montanus*). *Photochemical & Photobiological Sciences*, 19, 371–381.
 37. Dixit, A. S., Singh, N. S., & Sougrakpurn, R. (2014). A comparative study on photoperiodic control of seasonal cycles in the females of migratory yellow breasted bunting and the resident tree sparrow. *Photochemical & Photobiological Sciences*, 19, 371–381.
 38. Dixit, A. S., Byrsat, S., & Singh, N. S. (2020). Circadian rhythm in photoperiodic expressions of GnRH-I and GnIH regulating seasonal reproduction in the Eurasian tree sparrow, *Passer montanus*. *Journal of Photochemistry and Photobiology, B: Biology*, 211, 111993.
 39. Farner, D. S. (1964). The photoperiodic control of reproductive cycles in birds. *American Scientist*, 52, 137–156.
 40. Foster, R. G., & Soni, B. G. (1998). Extraretinal photoreceptors and their regulation of temporal physiology. *Reviews of Reproduction*, 3, 145–150.
 41. Foster, R. G., & Follett, B. K. (1985). The Involvement of a Rhodopsin-Like Photopigment in the Photoperiodic Response of the Japanese Quail. *Journal of Comparative Physiology. A, Sensory, Neural, and Behavioral Physiology*, 157, 519–528.
 42. Foster, R. G., Korf, H. W., & Schalken, J. J. (1987). Immunocytochemical markers revealing retinal and pineal but not hypothalamic photoreceptor systems in the Japanese quail. *Cell and Tissue Research*, 248, 161–167.
 43. Frisch, K. V. (1911). Beiträge zur Physiologie der Pigmentzellen in der Fischhaut. *Pflüger's Archiv für die gesamte Physiologie des Menschen und der Tiere*, 138, 319–387.
 44. Fu, Y., Zhong, H., Wang, M. H., Luo, D. G., Liao, H. W., Maeda, H., Hattar, S., Frishman, L. J., & Yau, K. W. (2005). Intrinsically photosensitive retinal ganglion cells detect light with a vitamin A-based photopigment, melanopsin. *Proceedings of the National Academy of Sciences of the United States of America*, 102(29), 10339–10344.
 45. Gamlin, P. D., & Cohen, D. H. (1986). A second ascending visual pathway from the optic tectum to the telencephalon in the pigeon (*Columba livia*). *The Journal of Comparative Neurology*, 250, 296–310.
 46. Guadano-Ferraz, A., Obregon, M. J., St Germain, D. L., & Bernal, J. (1997). The type 2 iodothyronine deiodinase is expressed primarily in glial cells in the neonatal rat brain. *Proceedings of the National Academy of Sciences of the United States of America*, 94, 10391–10396.
 47. Gwinner, E. G., Turek, F. W., & Smith, S. D. (1971). Extraocular light perception in photoperiodic responses of the White-crowned sparrow (*Zonotrichia leucophrys*) and of the Golden-crowned sparrow (*Z. atricapilla*). *Zeitschrift für vergleichende Physiologie*, 75, 323–331.
 48. Haas, R., Alenciks, E., Meddle, S., & Fraley, G. S. (2017). Expression of deep brain photoreceptors in the Pekin drake: A possible role in the maintenance of testicular function. *Poultry Science*, 96, 2908–2919.
 49. Halford, S., Pires, S. S., Turton, M., Zheng, L., Gonzalez-Mendez, I., Davies, W. L., Peirson, S. N., Garcia-Fernandez, J. M., et al. (2009). VAopsin-based photoreceptors in the hypothalamus of birds. *Current Biology*, 19, 1396–1402.
 50. Hannibal, J., & Fahrenkrug, J. (2004). Target areas innervated by PACAP-immunoreactive retinal ganglion cells. *Cell and Tissue Research*, 316, 99–113.
 51. Hartwig, H. G. (1974). Electron microscopic evidence for a retinohypothalamic projection to the suprachiasmatic nucleus of *Passer domesticus*. *Cell and Tissue Research*, 153, 89–99.
 52. Hojvat, S., Baker, G., Kirsteins, L., & Lawrence, A. M. (1982). Growth-Hormone (Gh) Immunoreactivity in the Rodent and Primate Cns - Distribution. *Characterization and Presence Post-Hypophysectomy*. *Brain Res.*, 239, 543–557.
 53. Homma K and Sakakibara Y 1971 Encephalic photoreceptors and their significance in photoperiodic control of sexual activity in Japanese quail; in *Biochronometry* (ed) M Menaker (Nat. Acad. Sci., Washington) pp 333–341
 54. Homma, K., Wilson, W. O., & Siopes, T. D. (1972). Eyes Have a Role in Photoperiodic Control of Sexual Activity of Coturnix. *Science*, 178, 421–423.
 55. Ishibashi, T. (1957). *Studies on the effects of the artificial illumination upon the development of the gonad in the fowl* (p. 3). Sci Rep Hyogo Univ Agr.
 56. Kang, S. W., Leclerc, B., Kosonsiriluk, S., Mauro, L. J., Iwasawa, A. E., & Halawani, M. E. (2010). Melanopsin expression in dopamine-melatonin neurons of the premammillary nucleus of the hypothalamus and seasonal reproduction in birds. *Neuroscience*, 170, 200–213.
 57. King, J. R., Follett, B. K., Farner, D. S., & Morton, M. L. (1966). Annual Gonadal Cycles and Pituitary Gonadotropins in *Zonotrichia Leucophrys Gambelii*. *Condor*, 68, 476–487.
 58. Knight, P. G., Cunningham, F. J., & Gladwell, R. T. (1983). Concentrations of immunoreactive luteinizing hormone releasing hormone in discrete brain regions of the cockerel: Effects of castration and testosterone replacement therapy. *Journal of Endocrinology*, 96, 471–480.
 59. Konishi, H., Iida, K., Ohta, M., & Takahashi, M. (1988). A possible role for the eyes in the photoperiodic response of quail. *General and Comparative Endocrinology*, 72, 461–466.
 60. Konishi, H., Wada, M., & Homma, K. (1985). Retinal Modulation of the Hypothalamic Sensitivity to Testosterone Feedback in Photoperiodism of Quail. *General and Comparative Endocrinology*, 59, 343–349.
 61. Korenbrot, J. I., & Fernald, R. D. (1989). Circadian rhythm and light regulate opsin mRNA in rod photoreceptors. *Nature*, 337, 454–457.
 62. Ksendzovsky, A., Pomeranic, I. J., Zaghoul, K. A., Provenccio, J. J., & Provenccio, I. (2017). Clinical implications of the melanopsin-based non-image-forming visual system. *Neurology*, 88(13), 1282–1290.
 63. Langel, J. L., Smale, L., Esquivia, G., & Hannibal, J. (2015). Central melanopsin projections in the diurnal rodent. *Arvicanthis niloticus*. *Front. Neuroanat.*, 9, 93.
 64. Maddineni, S., Ocon-Grove, O. M., Krzysik-Walker, S. M., Hendricks, G. L., Proudman, J. A., & Ramachandran, R. (2008). Gonadotrophin-inhibitory hormone receptor expression in the chicken pituitary gland: Potential influence of sexual maturation and ovarian steroids. *Journal of Neuroendocrinology*, 20, 1078–1088.
 65. Majumdar, G., Yadav, G., Rani, S., & Kumar, V. (2014). A photoperiodic molecular response in migratory redheaded bunting exposed to a single long day. *General and Comparative Endocrinology*, 204, 104–113.

66. Majumdar, G., Yadav, G., Rani, S., & Kumar, V. (2015). Bird eyes distinguish summer from winter: Retinal response to acute photoperiod change in the night-migratory redheaded bunting. *Journal of Chemical Neuroanatomy*, 68, 55–60.
67. Majumdar, G., Rani, S., & Kumar, V. (2015). Hypothalamic gene switches control transitions between seasonal life history states in a night-migratory photoperiodic songbird. *Molecular Cellular Endocrinology*, 399, 110–121.
68. Masuda, T., Iigo, M., Mizusawa, K., & Aida, K. (2003). Retina-type rhodopsin gene expressed in the brain of a teleost, ayu (*Plecoglossus altivelis*). *Zoological Science*, 20, 989–997.
69. Masumoto, K. H., Ukai-Tadenuma, M., Kasukawa, T., Nagano, M., Uno, K. D., Tsujino, K., Horikawa, K., Shigeyoshi, Y., & Ueda, H. R. (2010). Acute induction of Eya3 by late-night light stimulation triggers TSHbeta expression in photoperiodism. *Current Biology*, 20, 2199–2206.
70. Matsuo, H., Baba, Y., Nair, R. M., Arimura, A., & Schally, A. V. (1971). Structure of the porcine LH- and FSH-releasing hormone. I. The proposed amino acid sequence. *Biochemical and Biophysical Research Communications*, 43, 1334–1339.
71. McDonald, P. A. (1982). Influence of pinealectomy and photoperiod on courtship and nest-building in male doves. *Physiology & Behavior*, 29, 813–818.
72. Meier, A. H., & Farner, D. S. (1964). A possible endocrine basis for premigratory fattening in the white-crowned sparrow, *Zonotrichia leucophrys gambelii* (nuttall). *Gen. Com. Endocrinol.*, 4, 584–595.
73. Meier, R. E. (1973). Autoradiographic evidence for a direct retino-hypothalamic projection in the avian brain. *Brain Research*, 53, 417–421.
74. Menaker, M., & Keatts, H. (1968). Extraretinal light perception in the sparrow. II. Photoperiodic stimulation of testis growth. *Proceedings of the National Academy of Sciences of the United States of America*, 60, 146–151.
75. Millam, J. R., Craig-Veit, C. B., & Faris, P. L. (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.
76. Miyamoto, K., Hasegawa, 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.
77. Nakane, Y., Ikegami, K., Ono, H., Yamamoto, N., Yoshida, S., Hirunagi, K., Ebihara, S., Kubo, Y., & Yoshimura, T. (2010). A mammalian neural tissue opsin (Opsin 5) is a deep brain photoreceptor in birds. *Proceedings of the National Academy of Sciences of the United States of America*, 107, 15264–15268.
78. Nakao, N., Ono, H., Yamamura, T., Anraku, T., Takagi, T., Higashi, K., Yasuo, S., Katou, Y., et al. (2008). Thyrotrophin in the pars tuberalis triggers photoperiodic response. *Nature*, 452, 317–U311.
79. Ohta, M., & Homma, K. (1987). Detection of Neural Connection to the Infundibular Complex by Partial or Complete Hypothalamic Deafferentation in Male Quail. *General and Comparative Endocrinology*, 68, 286–292.
80. Ohuchi, H., Yamashita, T., Tomonari, S., Fujita-Yanagibayashi, S., Sakai, K., Noji, S., & Shichida, Y. (2012). A non-mammalian type opsin 5 functions dually in the photoreceptive and non-photoreceptive organs of birds. *PLoS ONE*, 7, e31534.
81. Oliver, J., & Bayle, J. D. (1975). Spontaneous and flash-induced multiple unit activity in the hypothalamic gonadotropic areas: Effects of photoperiod and of optic nerve section in quail. *Journal of Neuroscience Research*, 1, 475–484.
82. Oliver, J., Bouille, C., Herbute, S., & Bayle, J. D. (1978). Retrograde transport of horseradish peroxidase from the preoptic-anterior hypothalamic region to retinal ganglion cells in quail. *Neuroscience Letters*, 9, 291–295.
83. Orije, J. E. M. J., & Van der Linden, A. (2022). A brain for all seasons: An in vivo MRI perspective on songbirds. *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology*, 337(9–10), 967–984.
84. Osugi, T., Ukena, K., Bentley, G. E., O'Brien, S., Moore, I. T., Wingfield, J. C., & Tsutsui, K. (2004). Gonadotropin-inhibitory hormone in Gambel's white-crowned sparrow (*Zonotrichia leucophrys gambelii*): cDNA identification, transcript localization and functional effects in laboratory and field experiments. *Journal of Endocrinology*, 182, 33–42.
85. Palczewski, K., Kumasaka, T., Hori, T., Behnke, C. A., Motoshima, H., Fox, B. A., Le Trong, I., Teller, D. C., et al. (2000). Crystal structure of rhodopsin: A G protein-coupled receptor. *Science*, 289, 739–745.
86. Peirson, S. N., Halford, S., & Foster, R. G. (2009). The evolution of irradiance detection: Melanopsin and the non-visual opsins. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 364, 2849–2865.
87. Pepe, I. M. (2001). Recent advances in our understanding of rhodopsin and phototransduction. *Progress in Retinal and Eye Research*, 20, 733–759.
88. Pérez, J. H., Tolla, E., Dunn, I. C., Meddle, S. L., & Stevenson, T. J. (2019). A comparative perspective on extra-retinal photoreception. *Trends in Endocrinology and Metabolism*, 30(1), 39–53.
89. Pérez, J. H., Tolla, E., Bishop, V. R., Foster, R. G., Peirson, S. N., Dunn, I. C., Meddle, S. L., & Stevenson, T. J. (2023). Functional inhibition of deep brain non-visual opsins facilitates acute long day induction of reproductive recrudescence in male Japanese quail. *Hormones and Behavior*, 148, 105298.
90. Perfito, N., Jeong, S. Y., Silverin, B., Calisi, R. M., Bentley, G. E., & Hau, M. (2012). Anticipating Spring: Wild Populations of Great Tits (*Parus major*) Differ in Expression of Key Genes for Photoperiodic Time Measurement. *Plos One*, 7, 1.
91. Potter, H., Alenciks, E., Frazier, K., Porter, A., & Fraley, G. S. (2018). Immunolesion of melanopsin neurons causes gonadal regression in Pekin drakes (*Anas platyrhynchos domesticus*). *General and Comparative Endocrinology*, 256, 16–22.
92. Proudman, J. A., Scanes, C. G., Johannsen, S. A., Berghman, L. R., & Camp, M. J. (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.
93. Rebay, I., Silver, S. J., & Tootle, T. L. (2005). New vision from Eyes absent: Transcription factors as enzymes. *Trends in Genetics*, 21, 163–171.
94. Reinert, B. D., & Wilson, F. E. (1996). Thyroid dysfunction and thyroxine-dependent programming of photoinduced ovarian growth in American tree sparrows (*Spizella arborea*). *General and Comparative Endocrinology*, 103, 71–81.
95. Saab, S. S., Lange, H. S., & Maney, D. L. (2010). Gonadotropin-releasing hormone neurons in a photoperiodic songbird express fos and egr-1 protein after a single long day. *Journal of Neuroendocrinology*, 22, 196–207.
96. Saldanha, C. J., Deviche, P. J., & Silver, R. (1994). Increased VIP and decreased GnRH expression in photorefractory dark-eyed juncos (*Junco hyemalis*). *General and Comparative Endocrinology*, 93, 128–136.
97. Sharp, P. J., Talbot, R. J., Main, G. M., Dunn, I. C., Fraser, H. M., & Huskisson, N. S. (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.

98. Shen, W. L., Kwon, Y., Adegbola, A. A., Luo, J., Chess, A., & Montell, C. (2011). Function of Rhodopsin in Temperature Discrimination in *Drosophila*. *Science*, *331*, 1333–1336.
99. Sherwood, N. M., & Parker, D. B. (1990). Neuropeptide families: An evolutionary perspective. *Journal of Experimental Zoology. Supplement*, *4*, 63–71.
100. Shimizu, I., Yoshimoto, M., Kojima, T., & Okado, N. (1984). Development of retinohypothalamic projections in the chick embryo. *Neuroscience Letters*, *50*, 43–47.
101. Shimizu, M., & Bedecarrats, G. Y. (2006). Identification of a novel pituitary-specific chicken gonadotropin-releasing hormone receptor and its splice variants. *Biology of Reproduction*, *75*, 800–808.
102. Shimizu T and Karten, HJ 1991 Central visual pathways in reptiles and birds: Evolution of the visual system; in *Vision and Visual Dysfunction* (eds) JR Cronly-Dillo and RL Gregory (FL: CRC Press: Boca Raton) Vol. II. pp 421–441.
103. Sillman AJ 1973 Avian vision; in *Avian Biology* (eds) DS Farner and JR King (Academic Press, New York) Vol. III pp 349–387.
104. Silver, R., Witkovsky, P., Horvath, P., Alones, V., Barnstable, C. J., & Lehman, M. N. (1988). Coexpression of Opsin-Like and Vip-Like Immunoreactivity in Csf-Contacting Neurons of the Avian Brain. *Cell and Tissue Research*, *253*, 189–198.
105. Siopes, T. D., & Wilson, W. O. (1980). Participation of the Eyes in the Photosexual Response of Japanese Quail (*Coturnix Coturnix Japonica*). *Biology of Reproduction*, *23*, 352–357.
106. Slawski, B. A., & Buntin, J. D. (1995). Preoptic Area Lesions Disrupt Prolactin-Induced Parental Feeding-Behavior in Ring Doves. *Hormones and Behavior*, *29*, 248–266.
107. Smith, G. T., Brenowitz, E. A., & Wingfield, J. C. (1997). Roles of photoperiod and testosterone in seasonal plasticity of the avian song control system. *Journal of Neurobiology*, *32*, 426–442.
108. Soni, B. G., & Foster, R. G. (1997). A novel and ancient vertebrate opsin. *FEBS Letters*, *406*, 279–283.
109. Srivastava, U. C., & Gaur, P. (2013). Naturally occurring neuronal plasticity in visual wulst of the Baya weaver, *Ploceus philippinus* (Linnaeus 1766). *Cell and Tissue Research*, *352*(3), 445–467.
110. Stevenson, T. J., & Ball, G. F. (2012). Disruption of neuropsin mRNA expression via RNA interference facilitates the photoinduced increase in thyrotropin-stimulating subunit beta in birds. *European Journal of Neuroscience*, *36*, 2859–2865.
111. Sugiyama, S., Di Nardo, A. A., Aizawa, S., Matsuo, I., Volovitch, M., Prochiantz, A., & Hensch, T. K. (2008). Experience-dependent transfer of Otx2 homeoprotein into the visual cortex activates postnatal plasticity. *Cell*, *134*, 508–520.
112. Sun, Y. M., Flanagan, C. A., Illing, N., Ott, T. R., Sellar, R., Fromme, B. J., Hapgood, J., Sharp, P., Sealfon, S. C., & Millar, R. P. (2001). A chicken gonadotropin-releasing hormone receptor that confers agonist activity to mammalian antagonists - Identification of D-Lys(6) in the ligand and extracellular loop two of the receptor as determinants. *Journal of Biological Chemistry*, *276*, 7754–7761.
113. Surbhi and Kumar V., (2015). Avian photoreceptors and their role in the regulation of daily and seasonal physiology. *General and Comparative Endocrinology.*, *220*, 13–22.
114. Tabata, M., Suzuki, T., & Niwa, H. (1985). Chromophores in the extraretinal photoreceptor (pineal organ) of teleosts. *Brain Research*, *338*, 173–176.
115. Takagi, T., Yamamura, T., Anraku, T., Yasuo, S., Nakao, N., Watanabe, M., Iigo, M., Ebihara, S., & Yoshimura, T. (2007). Involvement of transforming growth factor alpha in the photoperiodic regulation of reproduction in birds. *Endocrinology*, *148*, 2788–2792.
116. Tarttelin, E. E., Bellingham, J., Hankins, M. W., Foster, R. G., & Lucas, R. J. (2003). Neuropsin (Opn5): A novel opsin identified in mammalian neural tissue. *FEBS Letters*, *554*, 410–416.
117. Tomonari, S., Takagi, A., Akamatsu, S., Noji, S., & Ohuchi, H. (2005). A non-canonical photopigment, melanopsin, is expressed in the differentiating ganglion, horizontal, and bipolar cells of the chicken retina. *American Associate Anatomical*, *234*, 783–790.
118. Tsutsui, K., Saigoh, E., Ukena, K., Teranishi, H., Fujisawa, Y., Kikuchi, M., Ishii, S., & Sharp, P. J. (2000). A novel avian hypothalamic peptide inhibiting gonadotropin release. *Biochemical and Biophysical Research Communications*, *275*, 661–667.
119. Tsutsui, K., Ubuka, T., Bentley, G. E., & Kriegsfeld, L. J. (2013). Review: Regulatory mechanisms of gonadotropin-inhibitory hormone (GnIH) synthesis and release in photoperiodic animals. *Frontiers in Neuroscience*, *7*, 60.
120. Ubuka, T., Bentley, G. E., Ukena, K., Wingfield, J. C., & 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.
121. Ubuka, T., Inoue, K., Fukuda, Y., Mizuno, T., Ukena, K., Kriegsfeld, L. J., & Tsutsui, K. (2012). Identification, expression, and physiological functions of siberian hamster gonadotropin-inhibitory hormone. *Endocrinology*, *153*, 373–385.
122. Underwood, H. (1985). Extraretinal photoreception in the lizard *Sceloporus occidentalis*: Phase response curve. *American Journal of Physiology*, *248*, R407–414.
123. Underwood, H., & Groos, G. (1982). Vertebrate circadian rhythms: Retinal and extraretinal photoreception. *Experientia*, *38*, 1013–1021.
124. Underwood, H., & Menaker, M. (1976). Extraretinal photoreception in lizards. *Photophysiology*, *23*, 227–243.
125. van Veen, T., Hartwig, H. G., & Müller, K. (1976). Light-dependent motor activity and photonegative behavior in the eel (*Anguilla anguilla* L.). *J. Com. Physiol.*, *111*, 209–219.
126. Vigh, B., Manzano, M. J., Zadori, A., Frank, C. L., Lukats, A., Rohlich, P., Szel, A., & David, C. (2002). Nonvisual photoreceptors of the deep brain, pineal organs and retina. *Histology and Histopathology*, *17*, 555–590.
127. Wada, Y., Okano, T., Adachi, A., Ebihara, S., & Fukada, Y. (1998). Identification of rhodopsin in the pigeon deep brain. *FEBS Letters*, *424*, 53–56.
128. Walls, G. L. (1942). The vertebrate eye and its adaptive radiation Bloomfield Hills, Michigan: Cranbrook Institute of Science. *J Nerv Ment Dis.*, *100*(3), 332.
129. Wang, G., & Wingfield, J. C. (2011). Immunocytochemical study of rhodopsin-containing putative encephalic photoreceptors in house sparrow, *Passer domesticus*. *General and Comparative Endocrinology*, *170*, 589–596.
130. Watanabe, T., Yamamura, T., Watanabe, M., Yasuo, S., Nakao, N., Dawson, A., Ebihara, S., & Yoshimura, T. (2007). Hypothalamic expression of thyroid hormone-activating and -inactivating enzyme genes in relation to photorefractoriness in birds and mammals. *American Journal of Physiology*, *292*, R568–R572.
131. Wilson, F. E. (1990). Extraocular control of seasonal reproduction in female tree sparrows (*Spizella arborea*). *General and Comparative Endocrinology.*, *77*, 397–402.
132. Wilson, F. E., & Reinert, B. D. (1995). A One-Time Injection of Thyroxine Programmed Seasonal Reproduction and Postnuptial Molt in Chronically Thyroidectomized Male American Tree Sparrows *Spizella-Arborea* Exposed to Long Days. *Journal of Avian Biology*, *26*, 225–233.
133. Wilson, F. E., & Reinert, B. D. (2000). Thyroid hormone acts centrally to programme photostimulated male american tree sparrows (*Spizella arborea*) for vernal and autumnal components of Seasonality. *Journal of Neuroendocrinology*, *12*, 87–95.

134. Yamamura, T., Hirunagi, K., Ebihara, S., & Yoshimura, T. (2004). Seasonal morphological changes in the neuro-glial interaction between gonadotropin-releasing hormone nerve terminals and glial endfeet in Japanese quail. *Endocrinology*, *145*, 4264–4267.
135. Yamashita, T., Ohuchi, H., Tomonari, S., Ikeda, K., Sakai, K., & Shichida, Y. (2010). Opn5 is a UV-sensitive bistable pigment that couples with Gi subtype of G protein. *Proceedings of the National academy of Sciences of the United States of America*, *107*, 22084–22089.
136. Yaskin, V. A. (2011). Seasonal changes in hippocampus size and spatial behaviour in mammals and birds. *Zhurnal Obshchei Biologii*, *72*, 27–39.
137. Yasuo, S., Watanabe, M., Nakao, N., Takagi, T., Follett, B. K., 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.
138. Yokoyama, K., & Farner, D. S. (1976). Photoperiodic responses in bilaterally enucleated female white-crowned sparrows, *Zonotrichia leucophrys gambelii*. *General and Comparative Endocrinology*, *30*, 528–533.
139. Yoshimura, T., Yasuo, S., Watanabe, M., Iigo, 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*, 178–181.
140. Zhao, H., Jiang, J., Wang, G., Lee, C., & Wingfield, J. C. (2018). Daily, circadian and seasonal changes of rhodopsin-like encephalic photoreceptor and its involvement in mediating photoperiodic responses of Gambel's white-crowned Sparrow *Zonotrichia leucophrys gambelii*. *Brain Research*, *1687*, 104–116.

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