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Review

Circadian clocks and the measurement of daylength in seasonal reproduction

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A B S T R A C T

Temperate zone organisms measure changes in daylength to adapt to seasonal changes in their environment. Recent studies have revealed that the long day (LD)-induced thyrotropin (TSH) in the pars tuberalis (PT) of the pituitary gland act as a master factor regulating seasonal reproduction on the the ependymal cells (ECs) within the mediobasal hypothalamus (MBH) to induce expression of type 2 deiodinase (Dio2), a thyroid hormone (TH)-activating enzyme in both LD and short day (SD) breeders. Locally activated TH in the MBH is believed to trigger GnRH secretion from the hypothalamus in LD breeders, while it terminates reproductive activity in SD breeders. Circadian clock is involved in seasonal time measurement and clock genes are expressed in the PT and ECs. Although circadian and melatonin-dependent control of TSH appears to link the circadian clock and the photoperiodic response in mammals, how this circadian clock measure daylength remains to be clarified.

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1. Introduction

Organisms living outside the tropics predict seasonal changes in their environment and accordingly adapt their physiology and behavior, such as reproduction, migration, hibernation, and molt. Although temperature and precipitation show annual changes, changes in daylength (photoperiod) are the most reliable seasonal cue, because solstices and equinoxes occur at almost identical times each year. Therefore, it is plausible that organisms use changes in photoperiod as a calendar; this phenomenon is called photoperiodism (Garner and Allard, 1920; Rowan, 1925). Adaptation to the seasons also involves phases of reproduction, because seasonal reproduction maximizes the survival of offspring. For example, hamsters and birds with gestation or incubation periods of several weeks duration breed during the spring and are so-called long-day (LD) breeders. In contrast, goats and sheep have a gestation period of ~6 months and breed during the fall and are, therefore, so-called short-day (SD) breeders. In both LD and SD breeders, offspring are born and raised during spring and summer when the climate is moderate and food is abundant.

Seasonal reproduction is regulated by the hypothalamic–pituitary–gonadal (HPG) axis such that seasonal breeders experience annual cycles of reproductive quiescence and renaissance. GnRH secretion from the hypothalamus, and hence gonadotropin (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]) secretion from the anterior pituitary, is activated during the breeding season, resulting in a dramatic change in gonadal size. Amongst

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the various vertebrates, birds have highly sophisticated photoperiodic mechanisms, and their gonadal size changes more than a hundred-fold. This robust response, as well as their restricted breeding season, may be examples of the adaptations of birds to flight. Accordingly, birds were often used to study photoperiodism. Amongst mammals, hamsters and sheep are often used in such studies, because they also show robust photoperiodic responses. However, the magnitude of gonadal changes is less dramatic in mammals than in birds, and only involves a change of several-fold. Here, we review current understanding of the mechanisms of regulation of seasonal reproduction in birds and mammals in relation to the circadian clock.

2. Involvement of the circadian clock in photoperiodic time measurement

When hamsters kept under SD conditions are transferred to various longer daylength conditions, testicular recrudescence can be seen only for those hamsters transferred to photoperiods of 12.5 h or longer (Elliott, 1976; Goldman, 2001). In Japanese quail, daylength longer than 11.5 h induces testicular growth (Follett and Maung, 1978). Thus, these photoperiods are said to be the "critical photoperiod" to induce the photoperiodic response. It has also been demonstrated in quail that brief light pulses interrupting long nights of SD conditions also induce a photoperiodic response, but this response could be observed at a specific time of day, called the "photoinducible phase" (Follett and Sharp, 1969). In house finch and quail, a 6-h light period coupled with dark periods of varying duration (resonance light cycles) does not cause the photoperiodic response in cycle lengths that are multiples of 24 h (e.g. 6 h light, 18 h dark: 6L18D, 6L42D, 6L66D), but causes a photoperiodic response in cycle lengths that are not multiples of 24 h (6L30D, 6L54D) (Hamner, 1963; Follett and Sharp, 1969) (Fig. 1). In such experiments, the 6 h of light exposure would occur at the same phase of day in light cycles that are multiples of 24 h, while the 6-h light exposure would occur at different phases of the day in non-24-h cycles. Similar observations were also reported in golden hamsters (Elliott et al., 1972). All of these observations clearly suggest the involvement of the circadian clock in photoperiodic time measurement.

3. Eyes, the suprachiasmatic nucleus, and melatonin are essential for seasonal reproduction in mammals, but not in birds

In mammals, the eyes are believed to be the only photoreceptor organs, and removal of the eyes abolishes the photoperiodic response (Reiter, 1980). The master circadian pacemaker is localized in the suprachiasmatic nucleus (SCN) in mammals (Inouye and Kawamura, 1979; Ralph et al., 1990). Light stimulation received by the eyes is transmitted to the pineal gland via the SCN (Reiter, 1980; Arendt, 1995) (Fig. 2). From the pineal gland, melatonin is secreted during the night; the melatonin secretion profile encodes the night length. Melatonin plays a deterministic role in the regulation of seasonal reproduction in mammals; pinealectomy abolishes seasonal responses, while melatonin administration restores them in both LD and SD breeders (Hoffman and Reiter, 1965; Reiter, 1980; Arendt, 1995). Melatonin has been demonstrated to enter cerebrospinal fluid (CSF) through the pineal recess, an evagination of the third ventricle (Tricoire et al., 2002). However, it is not clear whether melatonin carried to the brain by blood or CSF mediates the effect of photoperiod on reproduction. Because the SCN is required to generate nocturnal melatonin secretion profiles, SCN lesions also disrupt the photoperiodic response in mammals.

In birds, the master circadian pacemakers are located not only in the SCN but also in the eyes and the pineal organ (Ebihara and Kawamura, 1981; Takahashi and Menaker, 1982; Yoshimura et al., 2001; Steele et al., 2003). Relative significance of these three pacemakers is different among species. Pineal organ plays the predominant role in the house sparrow (Takahashi and Menaker, 1982), while eyes play a significant role in quail (Steele et al., 2003). In pigeon, the SCN plays a significant role as well as the pineal organ and the eyes (Yoshimura et al., 2001). Photoreceptors are also localized in multiple regions: the eye, the pineal organ, and the deep brain. In marked contrast to mammals, the photoperiodic response is not affected by removal of the eyes in duck (Benoit, 1935), lesions around the SCN (Davies and Follett, 1975), or pinealectomy (Siopes and Wilson, 1974) in quail. In addition, although melatonin is secreted during the night in birds as well as in mammals, melatonin has little or no importance in regulating

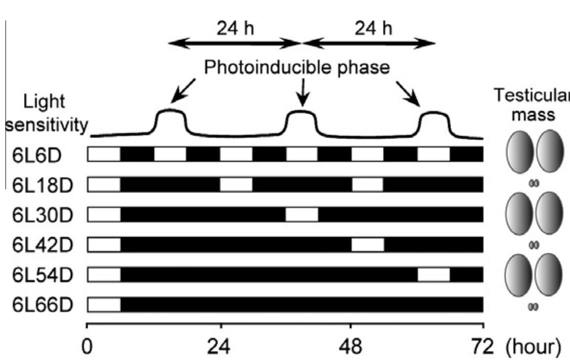

Figure 1. Light pulses given at a specific time of day called the "photoinducible phase" induce testicular growth in LD breeders, suggesting that the circadian clock is involved in photoperiodic time measurement.

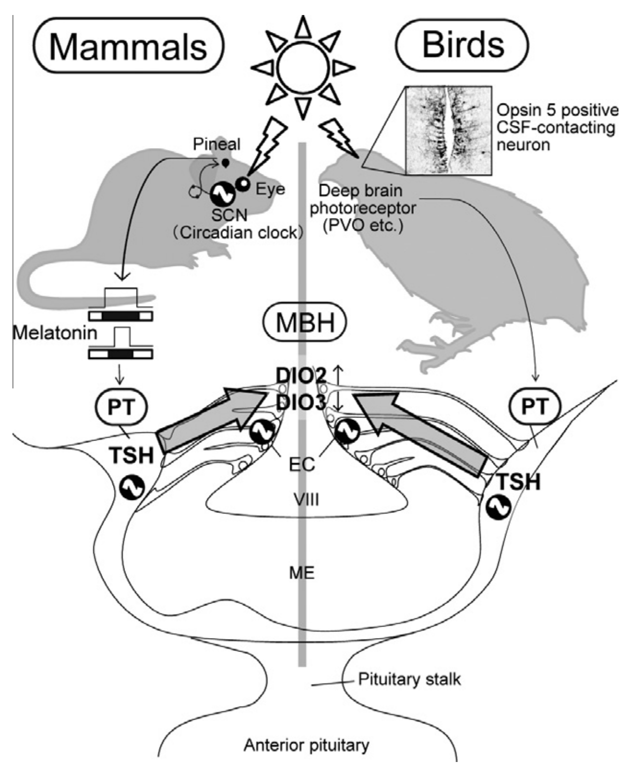

Figure 2. Photoperiodic signal transduction cascades in mammals and birds. Melatonin mediates transmission of photoperiodic information in mammals, while deep brain photoreceptors (e.g., Opsin 5) directly detect light within the brain, in birds. LD-induced pars tuberalis (PT) TSH acts on the ependymal cells (EC) to induce *Dio2* expression and reduce *Dio3* expression in both mammals and birds.