Circadian time-keeping system in birds: A review

Ila Mishra

Zoology Department, University of Delhi, Delhi- 110007

Abstract

In contrast to the highly centralised circadian clock in mammals, where the master clock resides in the anterior hypothalamic nucleus, as suprachiasmatic nucleus (SCN), the avian circadian timing machinery is more complicated with 3 circadian clock centres- the retina, hypothalamus and pineal. These three autonomous circadian oscillators interact with one another to regulate overt circadian rhythms in birds. Further, the contribution of each of these pacemakers is very diverse among different species. The homologue of mammalian SCN in birds is differentiated in two nuclei: medial SCN (mSCN) and the visual SCN (vSCN). Both mSCN and vSCN communicate through bidirectional and bilateral projections; allow them to communicate the light information with each other. Further, retinal photoreception via retinohypothalamic tract (RHT) is not the only photic input projected to the circadian clock machinery in birds. Many studies suggest that in birds, the entrainment of the endogenous circadian system by 24-hour light –dark (LD) cycles can persist even after enucleation. Circadian pacemaker in the pineal and in eyes of some avian species talks with the hypothalamic pacemaker via rhythmic synthesis and release of the melatonin hormone. In most of avian species, arhythmicity occurs following pinealectomy. Thus the disruption of circadian timing induced by pinealectomy support the hypothesis that the pineal is the locus of a major circadian pacemaker that controls the period and phase of other circadian oscillators and, in the absence of this pacemaker, the rest of the system is unable to maintain coherent circadian organization.

Keywords: Birds, SCN, pineal, retina, circadian, clock

1. Introduction

The organisms use circadian and circannual rhythms in individual cell or cell complexes for time keeping of clock. The biological clock system is required to anticipate the altered day/night cycles or changes in photoperiod. Organisms inhabiting outside the tropic experience the seasonal changes and accordingly adapt their physiology and behavior. The circadian clock operates within specialized oscillators with a period close to 24h in many behavioural functions. In birds circadian clock comprises of three component systems- the input, pacemaker and output connected to one another (Kumar et al., 2004). In the centre lies the clock (pacemaker) that intrinsically generates stable oscillations of precise cycle length.

The avian circadian clock system is more complex and diverse than mammals. The pacemaker that maintains the circadian time-keeping is present in the pineal gland, retina, and the SCN (which in birds consists of two different structures- the median SCN (mSCN) and visual SCN (vSCN; Brandstatter and Abraham, 2003). These components of the circadian timing machinery interact with one-another to regulate the downstream processes. Also, the contribution of these pacemakers is very diverse among different species. Further, peripheral rhythms have not been explored in birds as extensively as in mammals. However, many peripheral tissues are now known to express oscillator genes (Chong et al., 2003, Yoshimura et al., 2001).

2. Suprachiasmatic nucleus (SCN)

The avian circadian system is not solely regulated by SCN, instead other oscillatory components in the pineal or eyes are involved in circadian system. The homologue of mammalian SCN in birds is differentiated in two nuclei: medial SCN (mSCN) and the visual SCN (vSCN; Yoshimura et al., 2001). The location of mSCN is near the preoptic recess of the third ventricle and the vSCN is slightly more lateral and caudal to the mSCN. Both- mSCN and vSCN constitute the suprachiasmatic complex in birds and show functional equivalence to mammalian SCN. With the help of neuronal tracing method Cassone et al., proposed a model which states that photic information is transmitted to suprachiasmatic complex via three input pathways (Cantwell and Cassone, 2006). The perirotandal area and geniculate nuclei get the afferent projections from retinohypothalamic tract and further projects to vSCN. On the other hand, Yoshimura et al. hypothesised that extra retinal encephalic photoreceptor pathway give light input to mSCN in birds as one hour photic pulse during the subjective night induced per2 transcript in the mSCN of Japanese quail with eyes covered by opaque rubber caps (Yoshimura et al., 2001). Further, the role of extra retinal light transmission is corroborated by the reports showing expression of melanopsin protein in the lateral septal region as well as the hypothalamic periventricular region (Chaurasia et al., 2005).

Both mSCN and vSCN communicate through bidirectional and bilateral projections; allow them to communicate the light information with each other. Based on anatomical and physiological similarities between avian and mammalian structures and looking at distribution of retinohypothalamic projections (RHT), immunocytochemistry (Cassone and Moore, 1987) of the neural structures and rhythimicity in 2-deoxy [14C] glucose uptake (Cassone, 1988), and 2-[125I] iodomelatonin binding (Cassone and Brooks, 1991), vSCN is proposed to be an homologue of mammalian SCN (Cassone, 1991). On the other hand, some of the previous studies have suggested anatomical homology of mSCN to the mammalian SCN. Few studies have indicated that there is RHT projection to the mSCN (Norgren and Silver, 1989), and the mSCN lesions disrupted circadian rhythms in several avian species (Ebihara and Kawamura, 1981; Simpson and Follett, 1981; Takahashi and Menaker, 1982). Although the possibility remains that lesions included both mSCN and vSCN (Ebihara and Kawamura, 1981; Simpson and Follett, 1981; Takahashi and Menaker, 1982). Further, the expression of clock genes in avian hypothalamus was found specifically in mSCN, but not in vSCN. Lesion of mSCN further confirmed the role of mSCN in the circadian locomotor rhythmicity (Yoshimura et al., 2001).

3. Retinal clock

Light is considered as strongest zeitgeber and mainly perceived by eyes in most of the vertebrates. However, unlike the situation in mammals, retinal photoreception via retinohypothalamic tract (RHT) is not the only photic input projected to the circadian clock machinery in birds. Many studies suggest that in birds, the entrainment of the endogenous circadian system by 24-hour light –dark (LD) cycles can persist even after enucleation. For example, the bilateral orbital enucleation of sparrows resulted in entrained locomotor activity to light-dark cycles (reviewed in Menaker et al, 1997). This suggests that the circadian clock gets photic information directly from some other photosensory input, perhaps the encephalic photoreceptors.

The role of encephalic photoreceptors in photic entrainment has been shown in studies where the light penetration in the brain was blocked by capping the skull with carbon black in birds (reviewed in Menaker et al., 1997). Menaker's experiments suggested the role of encephalic photoreceptors in entrainment to light-dark cycles in sparrow. In another study on pigeon (*Columba livia*), the circadian rhythmicity was not abolished by pinealectomy or enucleation in constant dim light (LLdim). However, when pinealoctomy and enucleation both were done, the circadian rhythm in locomotor activity was abolished under prolonged LLdim conditions (reviewed in Ebihara et al., 1987). Further, light illumination only to eyes can potentially entrain the circadian melatonin rhythms (Underwood and Siopes, 1984; Underwood et al., 1990; Underwood, 1994) in Japanese quail, but not in pigeons. Also, the eyes of the chicken, Japanese quail and pigeons synthesise and secrete melatonin in a circadian fashion (reviewed in Brandstatter, 2002).

Further experiments on chicken and quail retinal clock provided evidence for existence of avian retinal autonomous clock. Steele et al. showed that quail eyes are coupled and work in synchrony with each other to drive circadian system (Steele et al., 2006). The ocular melatonin levels in both eyes were strongly coupled in Japanese quail with very low levels during the subjective day and high during the subjective night.

Further, the retinal clock function is accomplished via the photopigments. Candidate retinal photopigments including the melanopsin and its orthologues (see Natesan et al. 2002), the retinal pigment epithelium-derived rhodopsin homologue (peropsin, gRrh), and the retinal g-protein coupled receptor opsin (RGR-opsin, gRgr) are regulated in a circadian fashion. However, the role of these photopigments in the avian circadian clock system is still unrevealed (Surbhi et al., 2015).

4. Pineal gland

Pineal is the one of the pacemaker in avian circadian systems. The clock system needs an input to run the timekeeping with altered day and night. The light can be perceived via three different pathways: the eye, pineal and extra retinal photoreceptors located deep inside the brain. Circadian pacemaker in the pineal and in eyes of some avian species talks with the hypothalamic pacemaker via rhythmic synthesis and release of the melatonin hormone. The hypothalamic pacemaker is unable to maintain rhythmicity in constant conditions in the absence of rhythmic melatonin release from pineal (or eye). In avian circadian system there is a hierarchy in the relative roles of the pineal, the SCN, and the eyes in different species, in the pigeon circadian pacemaker in both pineal and eyes play the predominant role, while in Japanese quail the ocular pacemakers play the predominant role (Kumar, 2002).

The biological clock that resides within the avian pineal is not merely driving daily rhythms within the pineal organ but it can have a more important role. The clock within the avian pineal can act as a circadian “pacemaker”; that is, it can affect the animal’s entire circadian system. Gaston and Menaker (1968) were the first investigators to demonstrate a role for the avian pineal in circadian organization; they showed that removing the pineal of house sparrows expressing their endogenous circadian activity rhythm (free-running) in DD caused them to become arrhythmic. Pinealectomy has subsequently been shown to cause arrhythmicity in constant conditions (DD or dim LL) in many species of birds, including the house finches, spotted munia, Java sparrows, white-crowned sparrows, white throated, redheaded bunting sparrows, and starlings (Ebihara and Kawamura, 1981; Gaston and Menaker, 1968; Gwinner, 1978; McMillan, 1972; Pant and Chandola-Saklani, 1992). In most of these species arhythmicity occurs following pinealectomy, while in starlings only a few individuals exhibited arhythmicity and most showed a change in the period of the free-running rhythm (Gwinner, 1978). Thus there are species variations but mostly pinealectomy causes a major disruption of the circadian system. The data, therefore, support the hypothesis that the pineal is the locus of a major circadian pacemaker that controls the period and phase of other circadian oscillators and, in the absence of this pacemaker, the rest of the system is unable to maintain coherent circadian organization. A study by Zimmerman and Menaker (1979) offered substantial support to this hypothesis when they transplanted a pineal into the anterior chamber of the eye of a previously pinealectomized, arrhythmic birds and this synchronised the locomotor activity of the recipient with the activity of donor pineal.

5. Summary

The timing system that controls most biological rhythms in vertebrates is complex and is a composite of multiple pacemakers. In mammals, the cells in the SCN regulate most of the rhythmic functions that occur on a daily basis. Birds, on the other hand, have a highly complex and diverse clock system. Autonomous clocks in birds exist in at least three structures: the retina, the pineal gland and the hypothalamus. These appear to interact with each other, and form a central clock system (CCS). For evolutionary reasons, the role of hypothalamic clock seems consistent in all species (Ebihara & Kawamura, 1981; Ebihara et al., 1987), but that of the pineal and retinal clocks appear species-specific (e.g., retinas are the critical component of the circadian system of the quail but not of the house sparrow; see Kumar, 2002). Overall, the circadian system is plastic and the existence of multiple clocks helps them to stabilize/amplify each other in order to produce a highly stable circadian output

(Kumar and Singh, 2005). Since one of the fundamental properties of circadian organization is to be adaptive, it is logical to assume that the avian central circadian system will be diverse at the species level, since birds inhabit varied environments.

References

- Brandstatter R., 2002. The circadian pacemaking system in birds. In Biological rhythms, Kumar V., (Eds). Pp 144-163. Narosa Publishing House, Springer-Verlag.
- Brandstatter R., Abraham U., 2003. Hypothalamic circadian organization in birds. I. Anatomy, functional morphology, and terminology of the suprachiasmatic region. Chronobiol. Int. **20**: 637–655.
- Cantwell E.L., Cassone V.M., 2006. Chicken suprachiasmatic nuclei: II. Autoradiographic and immunohistochemical analysis. J Comp Neurol. 499: 442–457.
- Cassone V.M, Brooks D.S., 1991. Sites of melatonin action in the brain of the house sparrow, *Passer domesticus*. J Exp Zool. 260: 302–309.
- Cassone V.M., 1991. Melatonin and suprachiasmatic nucleus function. In: Suprachiasmatic Nucleus: The Mind's Clock, edited by Klein DC, Moore RY, and Reppert SM. New York: Oxford Univ. Press, p. 309–323.
- Cassone V.M., Moore R.Y., 1987. The retinohypothalamic projection and suprachiasmatic nucleus of the house sparrow, *Passer domestieus*. J Comp Neurol. 266:171-182.
- Chong N.W., Chaurasia S.S., Haque R., Klein D.C., Iuvone P.M., 2003. Temporal spatial characterization of chicken clock genes: circadian expression in retina, pineal gland, and peripheral tissues. J. Neurochem. **85**: 851–860.
- Ebihara S and Kawamura H., 1981. The role of the pineal organ and the suprachiasmatic nucleus in the control of circadian locomotor rhythms in the Java sparrow, *Padda oryzivora*. J Comp Physiol A. 141: 207–214.
- Ebihara S., Kawamura H., 1981. The role of the pineal organ and the suprachiasmatic nucleus in the control of circadian locomotorrhythms in the Java sparrow, Padda *oryzivora*. J Comp Physiol A. 141: 207–214.
- Ebihara S., Oshima I., Yamada H., Maki G., Koji S., 1987. Circadian organization in the pigeon. In: Hiroshige, T., Honma, K., eds. Comparative aspects of circadian clocks. Sapporo: Hokkaido University Press, pp. 84–94.
- Ebihara S., Oshima I., Yamada H., Maki G., Koji S.,1987. Circadian organization in the pigeon. In: Hiroshige, T., Honma, K., eds. Comparative aspects of circadian clocks. Sapporo: Hokkaido University Press, pp. 84–94.
- Gaston S., Menaker M., 1968. Pineal function: the biological clock in the sparrow? Science 160:1125–1127.
- Gwinner E., 1978. Effects of pinealectomy on circadian locomotor activity rhythms in European starlings, *Starnus vulgaris*. J Comp Physiol. 126: 123.
- Kumar V. 2002. Biological rhythms, Narosa Publishing House, Springer-Verlag.
- Kumar V., Singh B.P., 2005. The timekeeping system in birds. Proc Indian Nat Sci Acad B 5/6: 267–284.
- Kumar V., Singh B.P., Rani S., 2004. The bird clock: a complex multi-oscillatory and highly diversified system. Biol Rhythm Res **35**:121–144.
- McMillian JP., 1972. Pinealectomy abolishes the circadian rhythm of migratory restlessness. J Comp Physiol. 79:105.

- Menaker M., Moreira L.F., Tosini G., 1997. Evolution of circadian organization in vertebrates. Braz. J. Med. Biol. Res. 30, 305–313
- Natesan A.K., Cassone, V.M., 2002. Melatonin receptor mRNA localization and rhythmicity in the retina of the domestic chick, Gallus domesticus. Vis. Neurosci. 19: 265–274.
- Norgren R.B., Silver R., 1989. Retinohypothalamic projections and the suprachiasmatic nucleus in birds. Brain Behav Evol. 34: 73–83.
- Pant K, Chandola-Saklani A., 1992. Pinealectomy and LL abolished circadian perching rhythms but did not alter circannual reproductive or fattening rhythms in finches. Chronobiol Int. 9:413–420.
- Simpson S.M., Follett B.K., 1981. Pineal and hypothalamic pacemakers: their role in regulating circadian rhythmicity in Japanese quail. J Comp Physiol A. 144: 381–389.
- Steele T., Christopher, Tosini G., Siopes T., Underwood H., 2006. Time keeping by the quail's eye: Circadian regulation of melatonin production. Gen Comp Endocrinol. 145: 232–236.
- Surbhi, Kumar V., 2015. Avian photoreceptors and their role in the regulation of daily and seasonal physiology. Gen Comp Endocrinol. 220: 13-22.
- Takahashi J.S., Menaker M., 1982. Role of the suprachiasmatic nuclei in the circadian system of the house sparrow, *Passer domesticus*. J Neurosci. 2: 815–828.
- Underwood H., 1994. The circadian rhythm of thermoregulation in Japanese quail. Role of the eyes and pineal. J Comp Physiol A. 175: 639-653.
- Underwood H., Barett RK., Siopes T., 1990. Melatonin does not link the eyes t the rest of the circadian system in quail: a neural pathway is involved. J Biol Rhythms 5: 349-361.
- Underwood H., Siopes T., 1984. Circadian organisation in Japanese quail. J Exp Zool. 232: 557-566.
- Yoshimura T., Yasuo S., Suzuki Y., Makino E., Yokota Y., Ebihara S., 2001. Identification of the suprachiasmatic nucleus in birds. Am J Physiol 280: R1185–R1189.
- Zimmerman, N.H. and Menaker, M., 1979. The pineal gland: a pacemaker within the circadian system in the house sparrow. Proc. Natl. Acad. Sci. USA 76: 999-1003.