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Review

Chronobiology of reproduction in garter snakes: Neuroendocrine mechanisms and geographic variation

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ABSTRACT

The majority of studies on reproductive neuroendocrinology in snakes have focused on one particular snake population in Manitoba, Canada, the red-sided garter snake (*Thamnophis sirtalis parietalis*). Although traditionally these studies have emphasized its unusual temporal dissociation between mating behavior and peak gonadal activity, current evidence suggests that reproductive regulation in this population may be more similar to the norm than previously thought. Like other ectotherms, temperature plays a critical role in activating reproductive behavior in red-sided garter snakes. Diel melatonin and corticosterone rhythms appear to be important in transducing temperature cues, and it is clear that both hormones regulate courtship behavior during spring. Current evidence also suggests that sex steroid hormones are in fact central to reproductive regulation in males, although the timing of their action occurs during winter dormancy. Whether this is also true for female *T. sirtalis parietalis* requires further study, but it should be noted that patterns of sex steroid hormones are sexually dimorphic during winter dormancy, as are melatonin rhythms during spring emergence. While continuing to advance our understanding of reproductive regulation in this extremely well-studied population is prudent, future comparative studies are critical for understanding if and how reproductive regulatory mechanisms differ across environments, populations, and phylogenies. For example, melatonin and corticosterone responses to environmental cues vary significantly among populations of *T. sirtalis* in a common garden, as do male courtship behavior and androgen concentrations. These data support the hypothesis that neuroendocrine-mediated responses to environmental cues underlie phenotypic plasticity in reproductive life history traits.

1. Introduction

The ability to integrate and respond to environmental cues with appropriate physiology and behavior is crucial to the survival and reproductive fitness of all organisms. Most vertebrates exhibit seasonality in many processes, including feeding, immune function, aggression, and reproduction. Such seasonal cycles in physiology and behavior are thought to be a product of endogenous rhythms that are integrated with and entrained by environmental cues [32]. Collectively, these mechanisms constitute long-term timekeeping systems, and examples are widespread both in nature and across taxa.

Despite much research regarding the molecular biology of endogenous timekeeping (e.g., circadian rhythms), the mechanisms that integrate extrinsic environmental cues with intrinsic physiology and behavior are poorly understood. For example, it is not yet clear how seasonal changes in environmental cues are translated into meaningful neuroendocrine signals. Moreover, how do these neuroendocrine signals in turn induce changes in the hypothalamus–pituitary–gonad (HPG) axis to regulate reproductive physiology and behavior? Are evolutionary differences in these mechanisms at the route of observed differences in the timing and patterns of reproductive activity both between sexes and among populations?

My research aims to address these questions in a well-studied ectothermic model system, the common garter snake (*Thamnophis sirtalis*). The purpose of this review is to summarize the recent literature on the chronobiology of seasonal reproduction in this species and place it within the context of both historical perspectives and future research directions. Over the last 35 years, the reptilian garter snake system has become a remarkably powerful platform for understanding and integrating the ecology, physiology, endocrinology, and neuroethology of reproduction. Most of the available studies have focused on one particular population of snakes in Manitoba, Canada, the red-sided garter snake (*T. sirtalis parietalis*). As a result, we arguably know more about the environmental and neuroendocrine control of reproduction in this species than in any other reptile [14,28]. Continuing to advance our understanding of reproductive regulation in this extremely well-studied northern snake population is prudent, as research in this area will most quickly fill the gaps in our understanding of seasonal

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reproduction. However, future research directed at comparing regulatory mechanisms across taxa with different life history characteristics is critical for understanding if and how reproductive regulation differs among geographic populations. Such studies will provide valuable insights into the mechanisms governing phenotypic plasticity in reproductive life history traits and the evolution of reproductive regulatory mechanisms.

1.1. Model system and natural history

Thus far, research on the chronobiology of reproduction in garter snakes has compared three populations of *T. sirtalis*. The most northern population, the red-sided garter snake (*T. sirtalis parietalis*) in south central Manitoba, Canada, hibernates in underground dens for 8 months each year. Following spring emergence, male snakes remain near the den to engage in mate searching and courtship behavior during the attenuated 4-week mating season, as female snakes emerge 1–3 weeks later than males [12]. Red-sided garter snakes have been categorized as dissociated breeders because sex behavior and peak gonadal activity do not coincide temporally, as they tend to do in associated breeders (Fig. 1A; reviewed in [28]). Rather, mating behavior in *T. sirtalis parietalis* occurs while gonads are regressed and sex steroid hormones are relatively low (Fig. 1B; [8,10,36,61]). In addition, administration of hypothalamic, pituitary, or gonadal hormones does not initiate reproductive behavior in non-courting individuals [5,10,17,18,55]. Such dissociated reproductive patterns are thought to be an adaptation to environments that provide predictable but brief opportunities for reproduction [11,63]. Over time, the temporally dissociated reproductive pattern exhibited by red-sided garter snakes has been misinterpreted as demonstrating a complete dissociation of reproductive behavior from sex steroid hormone control. However, as proposed by Crews [9] and Saint Girons et al. [54], the current evidence discussed in this review suggests that sex steroid hormones act trans-seasonally to induce reproductive behavior (Fig. 1C).

In contrast to the abbreviated mating season exhibited by red-sided garter snakes, the mid-latitude red-spotted garter snake (*T. sirtalis concinnus*) in western Oregon has an extended breeding season lasting 10–12 weeks from March through May [44,47]. Similarly, southern-latitude eastern garter snakes (*T. sirtalis sirtalis*) in southern Florida also have an extended mating season and may be active during most of the year, as environmental conditions are extremely mild during winter months [57]. Both red-spotted and eastern garter snakes exhibit elevated androgen concentrations during spring, indicating that the testes are active and steroidogenic during the mating season [38,47,59]. These data suggest that reproductive behavior coincides with peak gonadal activity during the spring mating season, a phenomenon characteristic of associated reproductive patterns (Fig. 1A; [63]).

2. Environmental cues used in seasonal timekeeping

The most reliable environmental cue thought to function in regulating seasonality is photoperiod, as annual changes in day length accurately and reliably reflect changing seasons. In photoperiodic animals, changes in day length are registered and translated into precisely timed physiology and behavior [56]. For example, increasing day lengths are stimulatory to the reproductive axis of

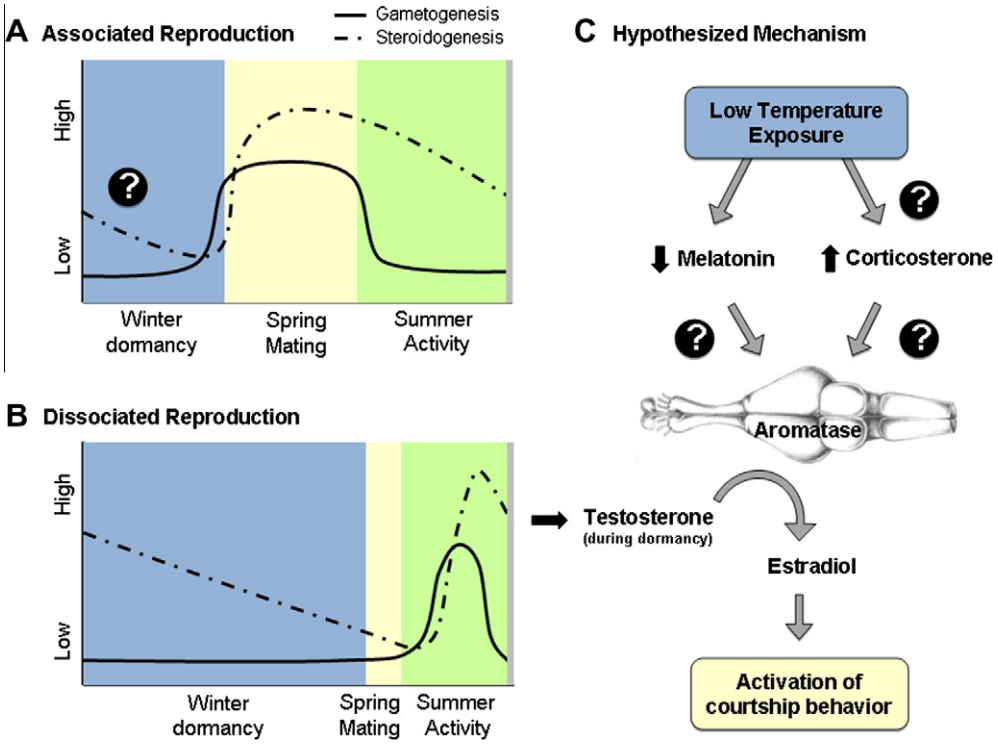

Fig. 1. Examples of seasonal relationships between mating, gametogenesis, and steroidogenesis in ectothermic vertebrates. In (A) associated or prenuptial breeders, mating behavior coincides with both gametogenesis and elevated sex steroid hormone concentrations. In (B) dissociated or postnuptial breeders such as the red-sided garter snake (*Thamnophis sirtalis parietalis*), there is a temporal dissociation between spring mating behavior, gametogenesis, and maximal sex steroid hormone concentrations. Many reptiles and amphibians do not fall discretely into these two categories, and intermediate patterns of reproductive activity are common. In red-sided garter snakes, the current hypothesized mechanism for temperature-induced activation of reproductive behavior is shown in (C). Elevated androgen concentrations during winter dormancy are aromatized in the brain to estrogens, and aromatase activity is critical for the initiation of male courtship behavior. Whether temperature-induced changes in melatonin and/or corticosterone modulate aromatase expression or activity requires further study. Note that we know exceedingly little about sex steroid hormone profiles during winter dormancy in species exhibiting associated or intermediate reproductive patterns. Thus, the mechanisms that appear to mediate temperature-induced reproduction in red-sided garter snakes may be more generally applicable than previously thought. Snake brain schematic redrawn from Krohmer et al. [25].