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Review

Sex or candy? Neuroendocrine regulation of the seasonal transition from courtship to feeding behavior in male red-sided garter snakes (*Thamnophis sirtalis parietalis*)

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ABSTRACT

This article is part of a Special Issue "Energy Balance".

Seasonal modulation of glucocorticoids plays an important role in supporting critical life-history events, and probably facilitates transitions between different life-history stages. In a well-studied population of red-sided garter snakes (*Thamnophis sirtalis parietalis*), glucocorticoids are elevated during the mating season, but males dispersing to summer feeding grounds have significantly lower baseline glucocorticoids than courting males at the den. We tested the hypothesis that decreased plasma glucocorticoids mediate the behavioral switch between reproduction and foraging in this species. Using a two-choice Y-maze paradigm, we demonstrate that males treated with the glucocorticoid synthesis inhibitor metyrapone (1 and 3 mg implants) prefer feeding cues (worm trail) over reproductive cues (female pheromone trail) significantly earlier than control-treated snakes. The metyrapone-induced changes in appetitive feeding behavior were independent of changes in plasma androgens and body mass loss. Metyrapone-treated males continued to court females at levels similar to those of control-treated snakes, suggesting that appetitive reproductive and ingestive behaviors are not mutually exclusive during this life-history transition. Consistent with this hypothesis, metyrapone treatment did not alter the number of arginine vasotocin-immunoreactive cells in any brain region, while it significantly increased neuropeptide Y-immunoreactive cell number in both the cortex and nucleus sphericus (homologues of the mammalian hippocampus and amygdala, respectively). Our results suggest that male red-sided garter snakes have the potential to maximize reproductive opportunities by continuing to court females they encounter even as they disperse from the den in search of food. Taken together, these data have important implications for understanding the neuroecology of seasonal life-history transitions.

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Introduction

A poorly understood aspect of regulatory biology is the nature of the neuroendocrine mechanisms that mediate transitions between life-history stages. Such transitions are often characterized by dramatic switches from one behavior mode to another and include examples such as reproduction, migration, and foraging. Behavioral switching helps organisms respond to and integrate the demands of the environment with their internal state, a process that is crucial to individual survival and reproductive fitness.

One hormone system that is thought to regulate life-history transitions is the hypothalamus–pituitary–adrenal (HPA) axis and its hormone product, glucocorticoids (see reviews in Landys et al., 2006; Romero, 2002; Wada, 2008). Because the HPA axis functions in energy homeostasis, it provides a mechanism by which information about an individual's internal state can be incorporated into "decisions" regarding reproduction, aggression, parental care, migration, and foraging, among others. Glucocorticoids also have the capacity to modulate a wide variety of physiological and behavioral functions. For example, glucocorticoids can modify metabolism, mobilize energy stores, and alter behavior during periods of high-energy demand (Astheimer et al., 1992; McEwen and Wingfield, 2003).

Current data indicate that seasonal modulation of plasma glucocorticoids plays an important role in supporting critical life-history events, and probably facilitates life-history transitions (e.g., Landys et al., 2006; Moore and Jessop, 2003; Wada, 2008). Correlated changes in activity levels and elevated baseline glucocorticoid concentrations are well documented in many vertebrates and include such examples as avian migratory flight and anuran vocalization (e.g., Emerson and Hess, 2001; Holberton, 1999; Landys-Ciannelli et al., 2002; Leary and Harris, 2013; Leary et al., 2006; Piersma et al., 2000; Reneerkens et al., 2002). Seasonal changes in reproductive behaviors also appear to be supported by elevated baseline glucocorticoids in a growing number of species (reviewed in Leary, 2009; Moore and Jessop, 2003; Romero, 2002). These and other studies demonstrate that seasonal variation in plasma glucocorticoids can be positively associated with seasonal changes in behavior, and suggest that the traditional view of glucocorticoids primarily as "stress hormones" is incomplete (e.g., McEwen and Wingfield, 2003). Unfortunately, data examining the influence of seasonal and intraseasonal changes in plasma glucocorticoids on the neurobiology of life-history transitions are lacking.

One life-history transition that is critically important to both individual survival and reproductive fitness is the tradeoff that often occurs between reproduction and foraging in animals. As reviewed by Schneider (2004) and Schneider et al. (2013), there is much overlap between the neuroendocrine mechanisms that control reproductive and ingestive behaviors. Dozens of different chemical messengers affecting food intake and/or sexual behavior have been described in vertebrates, particularly in rat and mouse models (Schneider et al., 2013). One current and pressing challenge is to better understand how these factors interact to mediate tradeoffs between appetitive and consummatory sexual and ingestive behaviors, particularly within physiologically- and ecologically-relevant contexts.

In the present study, we asked whether intraseasonal variation in baseline corticosterone concentrations, the primary glucocorticoid in reptiles, mediates the transition between reproduction and foraging in a well-studied population of red-sided garter snakes (*Thamnophis sirtalis parietalis*) in Manitoba, Canada. Specifically, we investigated possible interactions between plasma glucocorticoids and two neuropeptides that potently stimulate reproductive and ingestive behaviors: arginine vasotocin (AVT) and neuropeptide Y (NPY), respectively. The neuropeptide AVT and its mammalian homologue, arginine vasopressin (AVP), play a critical role in mediating reproductive behaviors in many vertebrates, often with complex sex- and context-dependent effects (see reviews in Godwin, 2010; Goodson and Bass, 2001; Wilczynski et al., 2005). In contrast, NPY is a highly conserved and potent orexigenic peptide that increases both appetitive and consummatory ingestive behaviors (e.g., preference for food cues, food hoarding, and/or food intake) in a variety of vertebrates, including red-sided garter snakes (Morris and Crews, 1990; see reviews in Matsuda et al., 2012; Mercer et al., 2011; Schneider et al., 2013).

In northern populations of *T. sirtalis parietalis*, snakes hibernate in underground dens for approximately 8 months each year. Following spring emergence, each population of red-sided garter snakes exhibits intense mating behavior for approximately 4 weeks. During this time, plasma corticosterone concentrations are elevated and sex steroid hormones tend to be low (reviewed in Krohmer and Lutterschmidt, 2011; Lutterschmidt, 2012). Female red-sided garter snakes generally disperse from the den post-copulation (usually within 1 day of emergence), but individual males remain near the den for several weeks, searching for mates and courting emerging females (Shine et al., 2001). Current data suggest that the duration of time an individual male exhibits courtship behavior is variable, ranging from just several days to more than 3 weeks (e.g., Lutterschmidt and Mason, 2008, 2009). After male and female snakes disperse from the den, they migrate up to 17 km to summer feeding areas (Gregory and Stewart, 1975). The factors regulating the seasonal transition from courtship to dispersal and feeding behavior are currently unknown, but multiple aspects of energy balance may be involved. For example, males do not eat during the mating season (Crews et al., 1987; Gregory and Stewart, 1975) and can lose up to 1% of their body mass per day during breeding (Shine et al., 2001). The lack of feeding behavior is not simply a result of limited food availability, as males will refuse food and choose courtship over feeding opportunities during the mating season (O'Donnell et al., 2004).

These studies suggest that the behavioral switch from reproduction to foraging is regulated by an endogenous signal. Cease et al. (2007) hypothesized that glucocorticoids play a critical role in this behavioral switch, as baseline corticosterone declines significantly during the mating season and is significantly lower in males migrating to summer feeding areas. These data suggest that elevated glucocorticoids are necessary to sustain sex behavior, and when glucocorticoids decrease to some threshold level, foraging behavior is activated (Cease et al., 2007). We tested this hypothesis by treating courting male red-sided garter snakes with metyrapone, an inhibitor of the enzyme steroid 11β-hydroxylase that is necessary for glucocorticoid synthesis in all vertebrates. We first asked if decreased plasma corticosterone induces the transition from courtship to feeding behavior, and examined if the changes in appetitive sexual and ingestive behaviors were associated with differences in androgen concentrations or body mass loss. In a second experiment, we used immunohistochemistry to examine if metyrapone-induced changes in courtship and feeding behaviors are associated with altered synthesis of the neuropeptides AVT and NPY in the brain. We hypothesized that a metyrapone-induced increase in appetitive ingestive behavior would be associated with increased NPY-immunoreactive cell number in the brain. Conversely, we hypothesized that decreased courtship behavior would be associated with a decrease in AVT-immunoreactive cell number.

Materials and methods

These experiments were conducted in the field with free-ranging red-sided garter snakes (*T. sirtalis parietalis*) in the Interlake region of

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