General and Comparative Endocrinology 227 (2016) 16–26

Contents lists available at ScienceDirect

General and Comparative Endocrinology

journal homepage: www.elsevier.com/locate/ygcen

Putting the brakes on reproduction: Implications for conservation, global climate change and biomedicine

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ARTICLE INFO

Article history:
Received 28 May 2015
Accepted 8 October 2015
Available online 22 October 2015

Keywords:
Reproduction
Birds
Gonadotropins
Gonadotropin-releasing hormone
Gonadotropin-inhibitory hormone
Environmental signals

ABSTRACT

Seasonal breeding is widespread in vertebrates and involves sequential development of the gonads, onset of breeding activities (e.g. cycling in females) and then termination resulting in regression of the reproductive system. Whereas males generally show complete spermatogenesis prior to and after onset of breeding, females of many vertebrate species show only partial ovarian development and may delay onset of cycling (e.g. estrous), yolk deposition or germinal vesicle breakdown until conditions conducive for ovulation and onset of breeding are favorable. Regulation of this "brake" on the onset of breeding remains relatively unknown, but could have profound implications for conservation efforts and for "mismatches" of breeding in relation to global climate change. Using avian models it is proposed that a brain peptide, gonadotropin-inhibitory hormone (GnIH), may be the brake to prevent onset of breeding in females. Evidence to date suggests that although GnIH may be involved in the regulation of gonadal development and regression, it plays more regulatory roles in the process of final ovarian development leading to ovulation, transitions from sexual to parental behavior and suppression of reproductive function by environmental stress. Accumulating experimental evidence strongly suggests that GnIH inhibits actions of gonadotropin-releasing hormones on behavior (central effects), gonadotropin secretion (central and hypophysiotropic effects), and has direct actions in the gonad to inhibit steroidogenesis. Thus, actual onset of breeding activities leading to ovulation may involve environmental cues releasing an inhibition (brake) on the hypothalamo-pituitary–gonad axis.

1. Introduction

Understanding the regulation of reproductive function is fundamental not only for biomedicine but also for agriculture, aquaculture, conservation and sustainability of natural bio-resources for harvest. In an age of burgeoning global change, elucidating the mechanisms underlying how organisms respond to environmental cues and regulate reproductive function become more and more important. To do this, it is essential that the reproductive process be analyzed at functional levels so that critical experiments can be designed. In this way we can gain insight into how environmental signals are perceived and then transduced through neural and neuroendocrine pathways into morphological, physiological and behavioral responses that maximize reproductive success (Visser, 2008; Wingfield, 2008a,b, 2012). Of particular importance is the integration of neuroendocrine and endocrine mechanisms with ecology and evolutionary biology to place neural pathways for environmental signals in context (e.g. MacDougall-Shackleton et al., 2009; Visser et al., 2010). As climate changes and phenology of migrations, breeding seasons, food supply, temperature, precipitation etc. shift, often in different ways, there is an increasing awareness that phenological mismatches are occurring more and frequently. For example, the great tit, *Parus major*, depends upon oak (*Quercus* sp) caterpillars in spring to feed young. The timing of caterpillar emergence in northern Europe is changing and some populations, but not all, of the great tit still breed at the same time resulting in a mismatch of environmental phenology and timing of

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http://dx.doi.org/10.1016/j.ygcen.2015.10.007
0016-6480/

breeding (e.g. Visser et al., 2012). Why does this mismatch occur in some populations and not others? The great tits showing a mismatch appear to be unable to respond to changed environmental signals and no longer time egg-laying, and thus the hatching of chicks, to coincide with the most favorable food supply.

Other investigations have shown variation in responsiveness to local predictive cues in terms of gonadal development. Lowland populations of song sparrows, *Melospiza melodia morphna*, are less sensitive to temperature cues affecting photoperiodically-induced gonadal growth than are high altitude populations (Perfito et al., 2005). In other species visual and tactile cues relating to food availability can enhance gonadal development (e.g. Hau et al., 2000; O'Brien and Hau, 2005; Furlonger et al., 2012) indicating that responsiveness, or not, to local environmental cues varies across populations and in some could lead to mismatches of food supply and reproductive function. What components of the "perception–transduction–response" system (Wingfield and Mukai, 2009) fail to adjust to changed phenology?

To answer these important and urgent questions will require careful analysis of phenology and the neural pathways for environmental signals in context (Visser et al., 2010). This review focuses primarily on songbird species, such as the white-crowned sparrow, *Zonotrichia leucophrys*, song sparrow, *Melospiza melodia*, and European starling, *Sturnus vulgaris*. They have been studied in considerable detail both from the perspective of their ecology and behavior under natural conditions and the neuroendocrinology and endocrinology of reproductive function. Such approaches have the potential to allow us to predict which populations will be able to cope with environmental change and which will not. Conservation efforts could thus be focused on the latter.

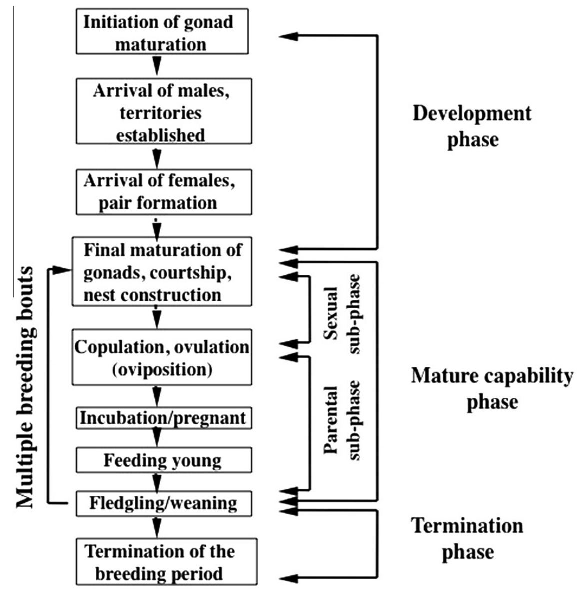

Fig. 1. The reproduction life history stage is made up of three distinct phases. First the development phase in which the gonads reach maturity and the animal is capable of reproduction. Second is the phase when actual onset of reproduction can take place. This may involve onset of estrus in mammals or yolk deposition leading to ovulation in egg-laying vertebrates. Parental care can be included in this phase. The third phase is termination of reproduction when cycling in females ceases and in many seasonally breeding animals the gonads regress. From Wingfield (2006), courtesy of Elsevier.

2. Environmental and endocrine regulation of the reproductive system

At mechanistic levels it is crucial to bear in mind that reproduction involves ontogenetic processes resulting in initial differentiation of the gonads and establishing sex (Crews and Moore, 1986; Wingfield, 2008a,b) followed by development of the reproductive system at puberty, and subsequently in seasonally breeding species, on a yearly basis. The ontogenetic development leading to initial establishment of male or female sex in Aves is not repeatable whereas annual development of the reproductive system in seasonal species is repeatable. This suggests fundamentally different regulatory mechanisms for these different events. However, developing a functional gonad is not the end point of the reproductive process, especially in females of tetrapods. For example, in avian species development of the gonad results in "mature capability" meaning that the individual is then capable of initiating a breeding attempt resulting in ovulation, copulation and in many species, raising of young. Moreover, in species that breed seasonally or periodically, reproductive function is terminated at the end of the breeding season and the gonads show morphological and physiological regression to varying degrees. Reproductive behaviors also frequently decline (Wingfield, 2008a).

A schematic diagram of the organization of the reproductive process in seasonally breeding birds and for many mammals is given in Fig. 1 (see Wingfield, 2006). Note the three phases of reproduction: development, mature capability (actual cycling of breeding attempts) and termination. Each phase may be regulated differently. The mature capability phase is perhaps the most complex because this involves onset of ovarian cycling in females leading to ovulation and mating (Fig. 1). In many avian and mammalian species there follows a period of parental care which can then lead to second breeding attempts, or if the nest and young are lost to predators, a replacement breeding attempt can be initiated (Fig. 1). Note that mature capability is entirely dependent upon the reproductive system being in a mature state so these nesting attempts – sexual and parental sub-phases – can be initiated (Fig. 1). There are some exceptions to this rule in mammals and other vertebrates (Crews and Moore, 1986), but this tends to be more uniformly so in birds.

We can now predict that multiple cues from the physical and social environments will regulate complex transitions between sexual and parental sub-phases of mature capability (Fig. 1). When reproductive development is complete and the individual has mature capability, onset of breeding does not necessarily occur immediately. In many species females are able to place a "brake" on final maturation leading to ovulation and subsequently the parental phase, until favorable cues from the physical and social environments release that brake. If those favorable cues do not occur then females can maintain the brake on onset of breeding indefinitely, or until the termination phase of reproductive function sets in. Therefore, it is possible that because of climate change, favorable conditions may not occur in some years, or the individual is no longer matched with those favorable conditions and females may even forego breeding for that year (e.g. Visser et al., 2010, 2012).

What environmental cues are used to regulate, and time, reproductive function? The literature is replete with hundreds, if not thousands, of reports indicating factors from physical and social environments that can influence the reproductive process. Firstly, initial predictive cues such as the seasonal change in day length are very reliable environmental cues that trigger reproductive development, sustain mature capability through the breeding season and then terminate reproductive function usually through gonadal regression (Fig. 2, see Dawson et al., 2001; Bentley et al., 2007; Yoshimura, 2004; Wingfield and Silverin, 2002, 2009). Then there are local predictive cues (supplementary factors) that speed up or slow down effects of initial predictive cues so that mature capability and onset of breeding can be timed accurately. Local