General and Comparative Endocrinology 188 (2013) 23–34

Contents lists available at SciVerse ScienceDirect

General and Comparative Endocrinology

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

Review

Neuropeptidergic regulation of reproduction in insects

Pieter Van Wielendaele, Liesbeth Badisco, Jozef Vanden Broeck *

Molecular Developmental Physiology and Signal Transduction, Department of Animal Physiology and Neurobiology, University of Leuven, Naamsestraat 59, P.O. Box 02465, B-3000 Leuven, Belgium

ARTICLE INFO

Article history:
Available online 26 February 2013

Keywords:
Insects
Regulatory peptides
Reproductive physiology
Neuroendocrinology

ABSTRACT

Successful animal reproduction depends on multiple physiological and behavioral processes that take place in a timely and orderly manner in both mating partners. It is not only necessary that all relevant processes are well coordinated, they also need to be adjusted to external factors of abiotic and biotic nature (*e.g.* population density, mating partner availability). Therefore, it is not surprising that several hormonal factors play a crucial role in the regulation of animal reproductive physiology. In insects (the largest class of animals on planet Earth), lipophilic hormones, such as ecdysteroids and juvenile hormones, as well as several neuropeptides take part in this complex regulation. While some peptides can affect reproduction via an indirect action (*e.g.* by influencing secretion of juvenile hormone), others exert their regulatory activity by directly targeting the reproductive system. In addition to insect peptides with proven activities, several others were suggested to also play a role in the regulation of reproductive physiology. Because of the long evolutionary history of many insect orders, it is not always clear to what extent functional data obtained in a given species can be extrapolated to other insect taxa. In this paper, we will review the current knowledge concerning the neuropeptidergic regulation of insect reproduction and situate it in a more general physiological context.

1. Introduction

Sexual reproduction enables metazoans to generate recombinant offspring and further develop the existing diversity of populations and species, promoting evolutionary adaptation and survival. In insects, but also in other metazoans, the highly complex process of sexual reproduction is composed of a sequence of multiple biological activities ranging from developmental to behavioral. The developmental processes that result in the gonadal production of mature gametes, already start during early embryogenesis and are tightly regulated by endo-, para- and autocrine factors. While some aspects of insect reproduction, such as courtship behavior, can be highly species-specific, others appear to be evolutionary more conserved. This implies that some genes involved in reproduction are evolving much faster than others involved in more conserved mechanisms. Thanks to molecular genetic studies, mechanisms underlying sex determination, reproductive organ development and sex-dependent differences in the central nervous system or CNS (‘brain sex’) that are associated with gender specific innate reproductive behaviors, have already been well documented in the fruit fly *Drosophila melanogaster* (Kimura et al., 2005). However, much less information is currently available on how the biological activities of different, spatially separated insect organs are coordinated and adjusted to internal and environmental conditions, in order to successfully produce viable offspring. The activity of these organs (*e.g.* CNS, fat body and gonads) is regulated by neural and endocrine systems, involving, amongst other communication signals, lipophilic hormones and neuropeptides (Fig. 1). The latter are peptidergic signaling molecules that are mainly produced by neurosecretory cells of the CNS (especially the brain), although they can also originate from other sources (neurons of the peripheral nervous system or non-neuronal endocrine cells) (Altstein and Nässel, 2010). An important insect neuroendocrine brain region that contains many neurosecretory cells, is the *pars intercerebralis* (PI). Neuropeptides produced by the PI are transported to specialized neurohemal structures, the *corpora cardiaca*, that store and timely release the neuropeptides into circulation (Altstein and Nässel, 2010; Ayali et al., 1996; Girardie et al., 1987, 1991).

The current paper will review the available information regarding the regulatory neuropeptides playing a role in insect reproductive physiology (Table 1). At first, we will discuss some important general aspects, such as the physiological link between feeding and reproduction, as well as the role of the lipophilic insect hormones, juvenile hormones and ecdysteroids, in the regulation of insect reproduction.

2. The role of lipophilic hormones in reproductive physiology

The ‘classic’ insect hormones, ecdysteroids and juvenoids, are well known for their role as important regulators of larval develop-

* Corresponding author. Fax: +32 16 32 39 02.
E-mail address: Jozef.VandenBroeck@bio.kuleuven.be (J. Vanden Broeck).

0016-6480/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ygcen.2013.02.005

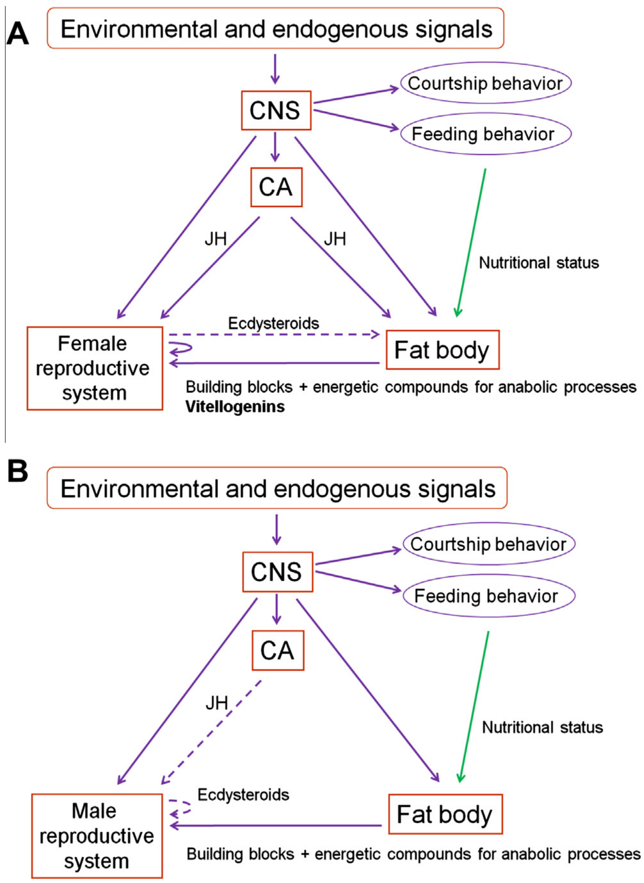

Fig. 1. Communication of key organs in female (A) and male (B) insect reproductive physiology. Maturation of reproductive tissues and production of gametes require energetic substrates and "building blocks" for anabolic processes, as well as vitellogenins (only in females), which are either stored in or produced by the fat body and which are transported to the reproductive tissues through circulation in the haemolymph. The fat body will only deliver these compounds upon a positive nutritional status, which is directly determined by the insect's feeding behavior. The central nervous system (CNS) perceives and processes endogenous as well as environmental signals, in function of which it coordinates an appropriate behavioral response and/or a response from the reproductive tissues and fat body. The reproductive tissues, fat body and CNS communicate by neural and endocrine systems that involve, amongst others, lipophilic hormones [ecdysteroids and juvenile hormone (JH)] and neuropeptides. Ecdysteroids are in adult insects produced by the gonads. In general, they positively control ovary and oocyte maturation and, at least in Dipteran species (**A**, dashed lines), they were demonstrated to stimulate vitellogenesis. JH is produced by the *corpora allata* (CA) and stimulates vitellogenin synthesis in the fat body as well as vitellogenin sequestration by the developing oocytes. Although not unambiguously proven (**B,** dashed lines), ecdysteroids and JH are suggested to positively influence spermatogenesis and maturation of the male reproductive system. (For a more detailed overview of the biological function of ecdysteroids and JH, the reader is referred to Sections 2.1 and 2.2). An important role in the steering of the above-described processes by the CNS is attributed to neuropeptide signaling systems. Neuropeptides either directly act upon the reproductive tissues and fat body to regulate tissue maturation, gametogenesis, ecdysteroidogenesis and/or vitellogenesis; or they do so indirectly by interaction with, or controlling synthesis of, lipophilic hormones or other communication signals. Furthermore, some of these peptides also regulate feeding behavior and might therefore (indirectly) influence the insect's nutritional status. This review will give an overview of the neuropeptides that have been associated with insect reproductive physiology and will illustrate how they fit in the (above) scheme.

ment and metamorphosis. However, both types of hormones are also involved in the regulation of reproduction in adult insects.

2.1. Ecdysteroids and reproductive physiology

The term "ecdysteroids" is the generic name for a group of structurally similar insect steroid hormones, of which ecdysone (E) and 20-hydroxyecdysone (20E) are the physiologically most important members (reviewed by Lafont and Koolman (2009) and Lafont et al. (2012)). In adults, ecdysteroids are mainly produced by the gonads (as reviewed by Brown et al. (2009)), although in some species other adult tissues also seem to secrete ecdysteroids (Delbecque et al., 1990; Gillott and Ismail, 1995). In the ovaries, ecdysteroids can serve diverse functions: (1) conjugates are stored in the eggs as a source of ecdysteroids during embryogenesis; (2) they can play autocrine or paracrine regulatory roles within the ovaries; (3) they can induce oocyte maturation (as progression of meiosis); (4) or be released as a hormone in the hemolymph leading to effects in other target tissues (*e.g.* induction of yolk protein synthesis in the fat body of higher Diptera (Huybrechts and De Loof, 1982), as reviewed by Simonet et al. (2004). Recent reports further document the role of the ovarian ecdysteroids, by demonstrating their involvement in differentiation of germ-line stem cells, development of follicle cells, oogenesis and ovary morphogenesis (Gancz et al., 2011; König et al., 2011; Parthasarathy et al., 2010; Ting, 2013). Moreover, ecdysteroids also appear to control the normal progression of oocyte growth cycles by regulating fat body autophagy (Bryant and Raikhel, 2011). Not only ovaries, but also insect testes can produce ecdysteroids (Brown et al., 2009; Loeb et al., 1997). However, the role of ecdysteroids in adult males has been less extensively documented than in adult females. According to some reports, ecdysteroids may be involved in the maturation of the male reproductive system, the regulation of spermatocyte differentiation (Dumser, 1980) and the mediation of sperm release from the testes (Polanska et al., 2009). In addition, these steroid hormones might also take part in the neural regulation of courtship behavior, both in males (Dalton et al., 2009; Ganter et al., 2011; Ishimoto et al., 2009) and females (Ganter et al., 2012).

2.2. Juvenile hormone and reproductive physiology

Juvenile hormone (JH), a sesquiterpenoid (category of isoprenoid-like compounds) produced by the *corpora allata* (CA), can occur in several forms in insects, although JH III is probably the most prevalent JH (Darrouzet et al., 1997; Goodman and Granger, 2005; Kotaki et al., 2009). In addition to its well-established role in preventing developmental progression to the adult stage, JH is also involved in the regulation of multiple aspects of insect metabolism, behavior, reproduction, diapause, migration, (caste) polyphenisms, immunity, stress tolerance and ageing (as reviewed by Simonet et al. (2004); Flatt et al. (2005) and Verma (2007)). In many species, JH is known to play a crucial stimulatory role in the control of vitellogenesis and to regulate vitellogenin sequestration by the growing oocytes by promoting patency of the surrounding follicle cells (Davey, 1981; Fei et al., 2005; Hartfelder, 2000; Tobe and Pratt, 1975). Furthermore, JH also appears to modulate female pheromone production in moths (Rafaeli and Bober, 2005; Rafaeli et al., 2003). Whereas the role of JH in female reproduction is well-studied, much less is known about its biological significance in male reproductive physiology. A role for JH in spermatogenesis has so far not been unambiguously proven. Nevertheless, the male accessory glands of some insect species are capable of synthesizing JH, either *de novo* (Borovsky et al., 1994) or by converting *corpora allata*-produced JH acid into JH (Shirk et al., 1976). As shown in some insect species, JH contained within the male accessory glands is transferred to the female during copulation, where it stimulates some reproductive events (Pszczolkowski et al., 2006; Shirk et al., 1980; Tian et al., 2010). JH was also shown to promote the production of secretory proteins in male accessory glands (Parthasarathy et al., 2009; Shemshedini et al., 1990). In addition, JH appears to promote male mating behavior (Wilson et al., 2003). Since JH is also involved in the control of behavior, caste polyphenism and