FROM BEHAVIOUR TO GENES: SEX IN THE JAPANESE QUAIL

by

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ABSTRACT

In Japanese quail (Coturnix japonica) like in most vertebrates, testosterone (T) activates male copulatory behaviour through its action in the preoptic area (POA). The transformation of T into estradiol by the enzyme aromatase localized in the POA is critical for this behavioral activation. We studied the distribution of aromatase in the quail brain and its regulation by steroids by radioenzyme assays on microdissected brain areas (quantification of enzymatic activity), by immunocytochemistry (visualization of the protein) and by RT-PCR/in situ hybridization (quantification and visualization of the corresponding mRNA). Partial cloning of the aromatase gene in quail also allowed us to produce a specific antibody to this enzyme raised against the quail sequence expressed in Escherichia coli. Aromatase synthesis in the POA is controlled at the pre-translational level by T and its metabolite estradiol, but estradiol receptors alpha (ERα) are not normally co-localized with aromatase. A new form of ER (ERβ) has been identified and we have recently cloned this receptor in quail. It is located in all brain regions that contain aromatase but whether ERβ is specifically present in aromatase-immunoreactive cells still needs to be investigated.

KEY WORDS: Aromatase, Estrogen synthase, Japanese quail, Sexual behaviour, Estrogen receptor beta, ERβ, in situ hybridization, RT-PCR, Preoptic area.

INTRODUCTION

Steroid hormones are lipophilic compounds derived from cholesterol that play a key role in the control of a large number of physiological and behavioral responses. Although a number or rapid actions at the membrane level have been described (see BAULIEU et al., 1999; SCHUMACHER, 1990; MCEWEN, 1994; RAMIREZ et al., 1996; MERMELSTEIN et al., 1996; see also below), steroids act mainly as factors that control genomic transcription. After binding to their specific intracellular receptors, steroids induce...
characteristic conformational changes in the receptor molecule. These changes then lead to processes such as the dimerization and/or phosphorylation of the receptor that can then interact with general and specific effector molecules, bind to specific DNA response elements in target genes and modulate their transcriptional activity (Wood et al., 1998; Landel et al., 1994, 1995; Uht et al., 1997). Many of these processes are tissue- and promoter-specific.

Sex steroids such as testosterone (T) in the male and estradiol or progesterone in the female are largely produced by the gonads. However, the brain is also capable of producing estrogens by a local conversion of androgens such as T or androstenedione into estradiol or estrone (fig. 1). The enzyme that catalyzes this reaction is a member of the P450 enzymes called aromatase or estrogen synthase and it was first identified in the brain in the early seventies (Naftolin et al., 1972, 1975). It was recently cloned in a number of mammalian species (gene CYP19) and is currently the subject of intensive research devoted to the control of its transcription (Simpson et al., 1991, 1994). The CYP19 gene is constituted of 10 exons including a first exon that is not translated and is tissue-specific. This tissue specificity seems to explain most of the differences that have been previously identified in the control mechanisms of aromatase activity as a function of the structure being studied (brain, adipose tissue, ovary, etc).

Fig. 1. Schematic illustration of the role of aromatase in the control of physiological responses to steroids. Testosterone that is synthesized from cholesterol enters its target cells and is transformed into estradiol (E₂) by the enzyme aromatase. E₂ then binds to estrogen receptors (ER) that can then dimerize and interact with estrogen-responsive elements (ERE) on specific genes to affect their transcription. The new proteins synthesized in this way will ultimately be responsible for the changes in cell physiology.