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## Hypothalamic control of the thyroïdal axis in the chicken: Over the boundaries of the classical hormonal axes

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### Abstract

The pituitary gland, occupying a central position in the hypothalamo-pituitary thyroïdal axis, produces thyrotropin (TSH), which is known to stimulate the thyroid gland to synthesize and release its products, thyroid hormones. TSH is produced by a specific cell population in the pituitary, the so-called thyrotropes. Their secretory activity is controlled by the hypothalamus, releasing both stimulatory and inhibitory factors that reach the pituitary through a portal system of blood vessels. Based on early experiments in mammals, thyrotropin-releasing hormone (TRH) is generally mentioned as the main stimulator of the thyrotropes. During the past few decades, it has become clear that the hypophysiotropic function of the hypothalamus is more complex, with different hormonal axes interacting with each other. In the chicken, it was found that not only TRH, but also corticotropin-releasing hormone (CRH), the main stimulator of corticotropin release, is a potent stimulator of TSH secretion. Somatostatin (SRIH), a hypothalamic factor known for its inhibitory effect on growth hormone secretion, was demonstrated to blunt the TSH response to TRH and CRH. In this review we summarize the latest studies concerning the “interaxial” hypothalamic control of TSH release in the chicken, with a special emphasis on the molecular components of these control mechanisms. It remains to be demonstrated if these findings could also be extrapolated to other species or classes of vertebrates. © 2005 Elsevier Inc. All rights reserved.

**Keywords:** Chicken; TSH; TRH; CRH; SRIH

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## 1. Introduction

The hypophyseal hormone thyrotropin (TSH) stimulates the thyroid gland to produce and release thyroid hormones, and hence it is responsible for the establishment of adequate thyroid hormone concentrations in the plasma. It was shown that bovine TSH is able to increase plasma thyroxine ( $T_4$ ) and 3,5,3'-triiodothyronine ( $T_3$ ) in immature chicks both in vivo and in vitro [1,2]. A central position in the hypothalamo-pituitary thyroidal (HPT) axis is taken by the thyrotropes, i.e. pituitary cells producing TSH. Thyrotropes are subject to various influences – both stimulating and inhibiting – originating in the hypothalamus. Traditionally thyrotropin-releasing hormone (TRH) is considered to be the main regulator of TSH secretion within the HPT axis. Recent research in the chicken however, has made it clear that the hypophysiotropic control of the hypothalamus is much more complex, with different hormonal axes interacting. Hypothalamic factors known to influence TSH release in the chicken include thyrotropin-releasing hormone, corticotropin-releasing hormone (CRH), and somatostatin (SRIH) (Fig. 1).

## 2. Thyrotropin-releasing hormone

Several researchers have demonstrated the presence of TRH in the avian brain [3,4]. Large quantities of TRH are evident in the hypothalamic area of the chicken and immunoreactive perikarya and neurons have been observed in the paraventricular nucleus and median eminence. These findings suggest a hypophysiotropic role for TRH in the chicken [4]. However, extrahypothalamic TRH, especially in the brain stem, accounts for approximately 70% of the total TRH content in the chicken brain, indicating that TRH may also act as a neurotransmitter or neuromodulator [4].

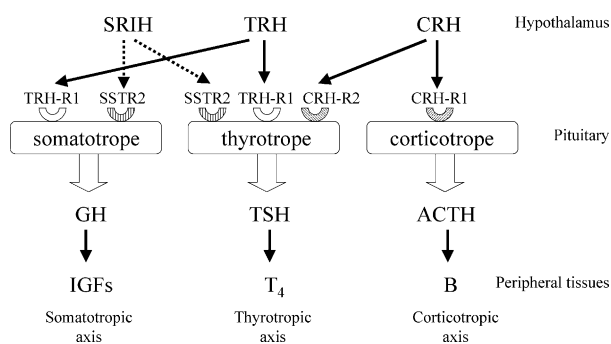


Fig. 1. Schematic representation of the multihormonal hypothalamic control of thyrotropin secretion in the chicken. Full arrows represent stimulatory interactions; dotted arrows are inhibitory interactions (ACTH: adrenocorticotrophic hormone; B: corticosterone; CRH: corticotropin-releasing hormone; CRH-R1: type 1 CRH receptor; CRH-R2: type 2 CRH receptor; GH: growth hormone; IGFs: insulin-like growth factors; SRIH: somatostatin; SSTR2: type 2 SRIH receptor;  $T_4$ : thyroxine; TRH: thyrotropin-releasing hormone; TRH-R1: type 1 TRH receptor; TSH: thyroid-stimulating hormone).

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