
Reviews

Involvement of the hypothalamic-pituitary-thyroid axis and its interaction with the hypothalamic-pituitary-adrenal axis in the ontogeny of avian thermoregulation: a review

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The emergence of thermoregulation in avian species is a complex matter in which neural as well as hormonal processes are involved. In a previous paper, the neural aspects of primary avian thermoregulation were discussed. In this paper the role of the hypothalamus-pituitary-thyroid axis (HPT-axis) and the hypothalamus-pituitary-adrenal axis (HPA-axis) in the ontogeny of avian thermoregulation is evaluated. The regulatory mechanisms and different important hormones of both axes, which have stimulatory or inhibitory effects, are discussed. Because the onset of functionality of the thermoregulatory system is of great interest, the ontogeny and functionality of the hormonal axes are clarified. There is a great difference between precocial and altricial birds in hormonal events as well as in neural processes which are involved in the emergence of thermoregulation. In precocial avian species the HPT-axis becomes functional during the mid- to late embryonic period while the same axis only becomes fully functional during the first week post-hatch in altricial avian species.

As early as the sixties, the emergence of homeothermy in chickens was investigated. It was concluded that the thyroid gland plays an important role in the thermoregulatory mechanisms of newly hatched chicks. More recent studies however were not able to show any direct effect of the thyroid hormones on the thermoregulation of day-old chicks, although blocking the conversion of T₄ to T₃ caused a decrease in body temperature in young chicks. Thyrotropin releasing hormone (TRH) is known to act in thermoregulation in mammals and several

authors have found an effect of TRH on the metabolism of young and older chicks. However, the exact mechanism still remains unclear.

Because the HPT- and the HPA-axis show close relationships, the role of the HPA-axis in the ontogeny of thermoregulation is also taken into consideration in this review. In mammals as well as in birds, corticotropin releasing hormone (CRH) is involved in the primary thermoregulation.

We conclude that the HPT-axis has an important role in the ontogeny of avian thermoregulation. The exact role of the HPA-axis remains largely unclear although at least CRH is definitely of some importance.

Keywords: thermoregulation; HPA-axis; HPT-axis; ontogeny; chicken

Introduction

The development of the thermoregulatory system in avian species is controlled by neural processes as well as by hormonal interactions. Baarendse *et al.* (2007) reviewed the neural aspect of the ontogeny of thermoregulation in both altricial and precocial birds. In addition, the role of the hypothalamic-pituitary-thyroid axis (HPT-axis) and the hypothalamic-pituitary-adrenal axis (HPA-axis) in this important event during the prenatal and perinatal life of birds has to be considered. Freeman (1964) was the first to assume that the thyroid hormones play an important role in the ontogeny of the thermoregulatory system in newly hatched chickens. More recent studies have shown the importance of thyroxine (T_4) and triiodothyronine (T_3) in thermal responses in chicks in the first weeks post hatching (Hwang-Bo *et al.*, 1990a), but the exact mechanism remains to be elucidated. The thyroid releasing hormone (TRH), produced by the hypothalamus, has also been found to induce thermoregulatory responses when administered intra-cerebroventricularly in neonatal chickens (Takahashi *et al.*, 2005). The HPT-axis and the HPA-axis show close interrelationship with one another, therefore, both axes will be discussed in this paper in relation to thermoregulation in early stages of development.

Regulatory mechanisms of the avian HPT-axis and the HPA-axis

The avian thyroid gland is primarily under control of the HPT-axis (*Figure 1*). The avian hypothalamus produces TRH and somatotropin release-inhibiting hormone (SRIH), which have a stimulatory and inhibitory effect, respectively, on the pituitary.

Energy demanding processes, such as cold exposure, primarily stimulate the hypothalamic paraventricular nucleus (PVN), leading to an increase in TRH synthesis and secretion (Arancibia *et al.*, 1996). TRH stimulates the thyrotrophs in the pars distalis of the adenohypofyse (the anterior lobe of the pituitary) thereby producing thyroid stimulating hormone (TSH), which interacts with the follicular cell membrane receptors in the thyroid gland. This results in the activation of adenylate cyclase and cAMP production ultimately leading to increased thyroid hormone (mainly T_4) synthesis and release (Hadley, 2000). The secretion of TSH by the pituitary is, besides hypothalamic TRH and SRIH regulation, modulated by a negative feedback mechanism of T_3 , which is produced locally by a specific type II-deiodinase monodeiodination of T_4 . This negative feedback on the hypothalamus is exerted by specific action of thyroid hormones on TRH producing neurons. Although TSH is the

major modulator of thyroid activity, thyroid hormone synthesis and secretion may be regulated by thyroid hormones in an autoregulatory manner (Greenspan and Rapoport, 1991).

Additionally, in response to stress, the hypothalamus produces corticotropin releasing hormone (CRH). CRH is the hypothalamic stimulatory regulator of adrenocorticotrophic hormone (ACTH), produced in the anterior pituitary. The release of ACTH stimulates the adrenal cortex, leading to an increase in corticosterone, a hormone that exerts a negative feedback on the hypothalamus as well as on the pituitary (Figure 1) (Carsia and Harvey, 2000).

CRH is also found to be a potent stimulator of TSH secretion. Indeed Geris *et al.* (1996) found that CRH also stimulates the production of TSH, through the specific CRH-receptor 2, by the anterior pituitary in 19-day-old chicken embryos, suggesting that there is a strong interaction between the HPT- axis and the HPA- axis already during prenatal stages. These findings illustrate the existence of an interaxial hypothalamic control of TSH release in chickens.

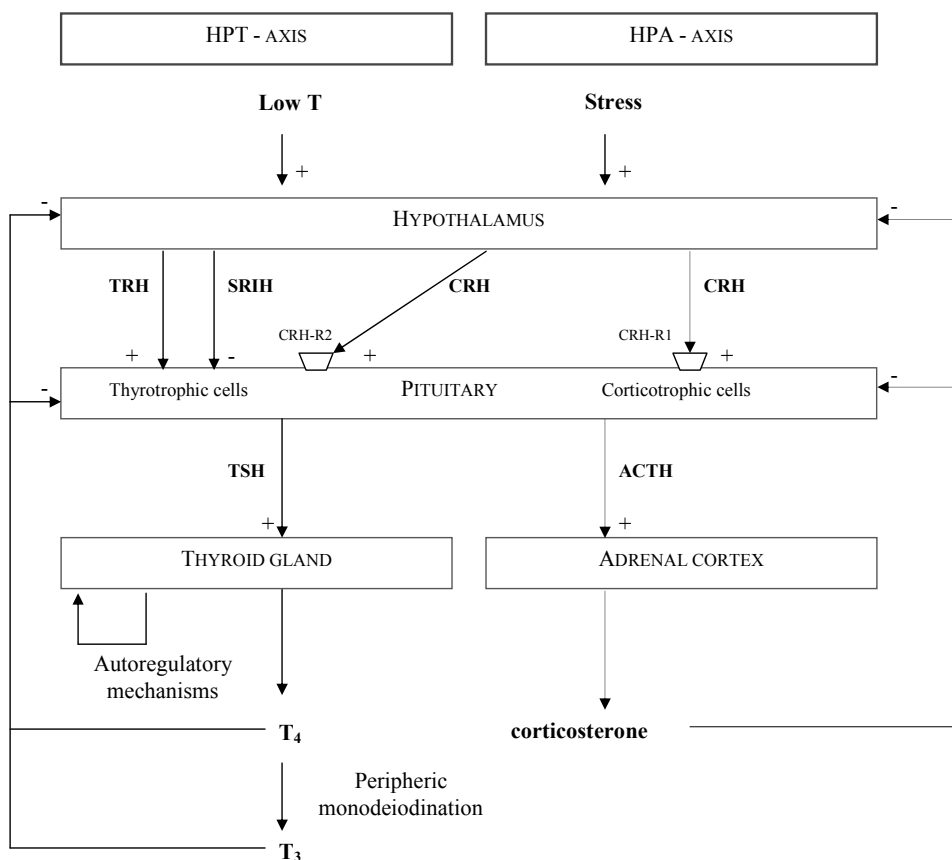


Figure 1 Regulatory mechanisms of the hypothalamic-pituitary-thyroid axis and the hypothalamic-pituitary-adrenal axis of the chicken. (T: temperature, TRH: thyrotropin releasing hormone, SRIH: somatotropin release-inhibiting hormone, TSH: thyroid stimulating hormone, T₄: thyroxine, T₃: triiodothyronine, CRH: corticotropin releasing hormone, ACTH: adrenocorticotrophic hormone, CRH-R: corticotropin releasing hormone receptor, '+' = stimulating effect, '-' = inhibitory effect).

The ontogeny of the Avian HPT-axis

HYPOTHALAMUS (TRH AND SRIH) AND PITUITARY (TSH)

Thommes *et al.* (1985) found that the number of TRH-positive perikarya increased gradually during day 6.5 to 13.5 of incubation of chicken embryos. During the critical period from embryonic day (ED) 11.5 to 16, functional maturation of the hypothalamus occurs, and interdependence of the HPT-axis is thought to emerge. A tenfold increase in hypothalamic TRH concentrations was observed between ED14 and day 1 post-hatch, whereas SRIH concentrations were only doubled towards the end of the incubation (Geris *et al.*, 1998). At hatch, hypothalamic TRH concentrations were increased twofold compared with internal pipping (Geris *et al.*, 1998).

In domestic animals and fowls the pituitary gland begins to form during embryonic life with two invaginations from the primitive mouth and the diencephalon, which differentiate into the adenohypophysis (or anterior pituitary) and the pars nervosa (or posterior pituitary). The avian adenopituitary has a characteristic morphology, consisting of the pars distalis, which is divided into two cytologically distinct areas (the cephalic and the caudal lobes), and the pars tuberalis, which bridges the median eminence and the anterior pituitary (Sasaki *et al.*, 2003). The anterior pituitary gland differentiates from Rathke's pouch into five distinct hormone-secreting cell types (Liu and Porter, 2004): corticotrophs, somatotrophs, thyrotrophs, gonadotrophs and lactotrophs. TSH producing cells or thyrotrophs are first observed on ED6.5 in the pars distalis of the chicken pituitary (Thommes *et al.*, 1983). The number of TSH cells increases progressively with developmental time. Conversely, TSH levels decreased from day 14 of incubation towards hatching, followed by a progressive increase during the post hatching period towards adulthood (Geris *et al.*, 1998).

THYROID GLAND: T₃ AND T₄

The functional components of the thyroid gland are formed by individual thyroid follicles, which consist of cuboidal epithelium arranged as a single layer surrounding a lumen (Hadley, 2000). In the chick embryo the thyroid gland originates as an evagination of the floor of the pharynx and divides into two lobes by day 5 of incubation (Shain *et al.*, 1972). At this time, the vascular supply of the thyroid gland is limited. At day 8 of incubation, blood vessels are uniformly distributed throughout the gland and by ED10 the sinusoidal vascular pattern reaches maximal development (Thommes, 1958). Thyroid follicles have been described by some investigators as being present on day 10 of incubation, while others have observed them on day 11 of incubation (Thommes and Tonetta, 1979). By ED15, the histology of the thyroid gland, as well as its vascular pattern, reaches full development.

The thyroid gland is able to regulate the net amount of iodide that is cleared from extracellular fluid and takes up the amount of iodine that is needed for thyroid hormone synthesis (Greenspan and Rapoport, 1991). At the luminal surface of the cell, iodide is incorporated into thyroglobulin, a very large glycoprotein molecule. Thyroglobulin is the precursor of the thyroid hormones (mainly T₄, T₃ is formed by peripherical monodeiodination of T₄) and is primarily stored in the colloid, a viscous gel in the follicular lumen. This extracellular pre-hormone storage in the colloid provides a large stock of potential thyroid hormone.

DIFFERENCES BETWEEN PRECOICIAL AND ALTRICIAL AVIAN SPECIES

In the precocial chicken and quail, the capacity of thyroid tissue to absorb iodine and/or synthesize thyroglobulin and thyroid hormones increases during the embryonic period (McNabb *et al.*, 1981; McNichols and McNabb, 1988). McNabb *et al.* (1981) observed

that thyroid and body weight increased proportionately from ED10 to ED15 (2.5-3.0-fold increase). The initiation of thyroid gland organization into follicles, and the rate of gland growth and follicle organization is remarkably slower in the altricial dove than in the precocial quail (McNabb and McNabb, 1977). In the altricial dove, only one third of the thyroid follicles were found to be active at the time of hatching. This altricial avian species was found to hatch with a relatively small thyroid gland followed by a rapid post hatching thyroid growth that paralleled with body growth (McNabb *et al.*, 1984; McNabb and Cheng, 1985).

It can be concluded that in the precocial chicken and quail alterations appear in the thyroidal capacity for iodine uptake and synthesis during the mid- and late embryonic period. In the altricial dove and blackbirds, on the other hand, thyroid function is low during the embryonic period, followed by a steady maturation during the first weeks post hatching (*Figure 2*).

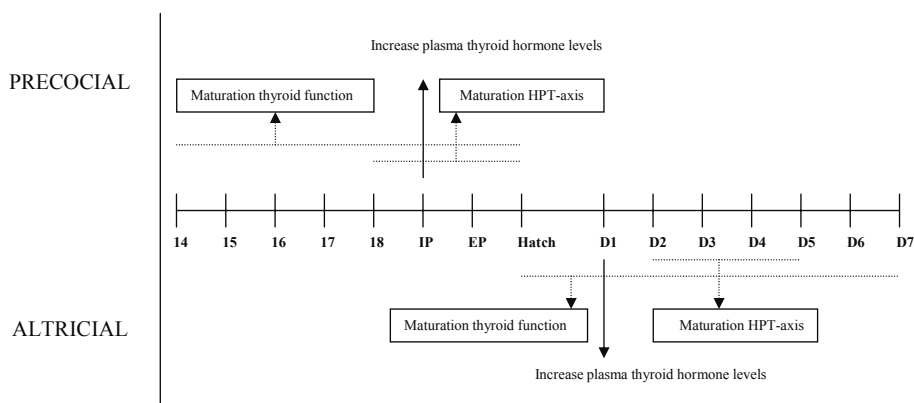


Figure 2 Differences in thyroid function and HPT-axis maturation between precocial and altricial avian species.

CIRCULATING T₃ AND T₄ CONCENTRATIONS DURING THE EMBRYONIC PERIOD AND THE FIRST WEEKS POST HATCHING: PRECOICIAL AVIAN SPECIES

In several precocial avian species the ontogenic pattern of total plasma thyroid hormone concentrations during the embryonic and post hatching period is well documented. Iodinated tyrosine molecules have been demonstrated within the developing chick thyroid gland at approximately the same time as the initial appearance of follicles (day 9-11 of incubation) (Daugères *et al.*, 1976). Thommes and Hylka (1978), however, showed that T₄ is already present in circulation as early as day 6.5 of incubation. Although thyroxine is detected, it is not clear whether these small amounts of T₄ in early embryos are of maternal or embryonic origin, or both. Prati *et al.* (1992) found thyroid hormones in the chicken's yolk and egg white at day 0 of incubation. The reported concentrations of T₄ (42 pg/g) and T₃ (11 pg/g) in the embryos at ED4 were lower than the concentrations of T₄ and T₃ in the egg yolk (3.8 ng/g and 1.5 ng/g, respectively) and egg white (0.07 ng/g and 0.06 ng/g, respectively) at day 0 of incubation. These results indicate that the yolk and albumen of the hen's egg contain maternal T₄ and T₃ and that these thyroid hormones are available to the developing embryo before onset of its own thyroid function. Although the thyroid gland is capable of concentrating iodine by at least day 5 of incubation, during the period of ED11-13, there is a significant increase in iodide uptake by the thyroid gland (Daugères *et al.*, 1976).

From that moment onwards, the thyroid gland is presumably the major, if not the only source for circulating thyroid hormones.

In the precocial domestic chicken and Japanese quail, plasma T_3 and T_4 concentrations are low during the mid-embryonic period, followed by a gradual increase and a peak value around the time of hatching (Thommes and Hylka, 1977, Decuypere *et al.*, 1982, McNabb and Hughes, 1983, Moraes *et al.*, 2004). Decuypere *et al.* (1982) reported a significant decrease of plasma T_4 concentrations after hatching (ED21-21.5). Plasma T_3 concentrations were found to increase during the first week post hatching followed by a stable period the week thereafter (Kühn *et al.*, 1982). Other authors however found a strong decrease of T_3 the day after hatching (McNabb and Hughes, 1983; McNichols and McNabb, 1988). The low circulating levels of T_3 during embryonic life and the sudden increase before hatching in the precocial chicken have been attributed to changes in the activity of hepatic iodothyronine deiodinases (Decuypere *et al.*, 1982). The most important change was the marked rise in the activity of type I 5'-deiodination, beginning the day before hatching, resulting in an increased conversion of T_4 into T_3 . From 10 days of age the concentrations of T_4 and T_3 did not significantly change as a function of age (day 10-21) (Spiers and Ringer, 1984).

Despite some variety in embryonic plasma thyroid levels in precocial birds, plasma T_4 hormones show the general pattern of increase during the mid- and late embryonic period. This elevation is followed by an increase in plasma T_3 concentrations just before hatching (*Figure 3*). Maximum values of both thyroid hormones occur around hatching. After hatching, both thyroid hormones decrease again, however T_4 returns to low embryonic levels and T_3 remains at a relatively higher level. Differences between the values of several studies in *Figure 3* can be due to the age of broiler breeders, different incubation parameters throughout the world or different genetic lines.

ALTRICIAL AVIAN SPECIES

In the altricial ring dove as well as in the European starling, total concentrations of both thyroid hormones (T_4 and T_3) were demonstrated to be low and remained unchanged during the embryonic period. No peak in thyroid concentration was reported in the dove and starling during the prenatal period (McNichols and McNabb, 1988; Výchob *et al.*, 2001). In several altricial species, plasma T_4 concentrations increased gradually during the first days post-hatching followed by a stable period. After a few days T_4 concentrations are comparable with the T_4 concentrations reported in the precocial Japanese quail (Výchob *et al.*, 1996). In ring doves, T_3 concentrations increase sharply during the first days post hatching and reach the same or even higher concentrations than reported in precocial species. Based on behavioural observations, McNabb and Cheng (1985) reported that dove nestlings were brooded almost continuously during the first 6 days but, at the age of 8 days, the parents spent most of the time off the nest, corresponding with the time when elevations of plasma thyroid concentrations take place. This could implicate that stabilization of body temperature coincides with an increase and levelling of thyroid hormone concentrations. Thyroid hormone concentrations steadily increased just prior to or coincident with the development of endothermy (McNabb *et al.*, 1984; McNabb and Cheng, 1985).

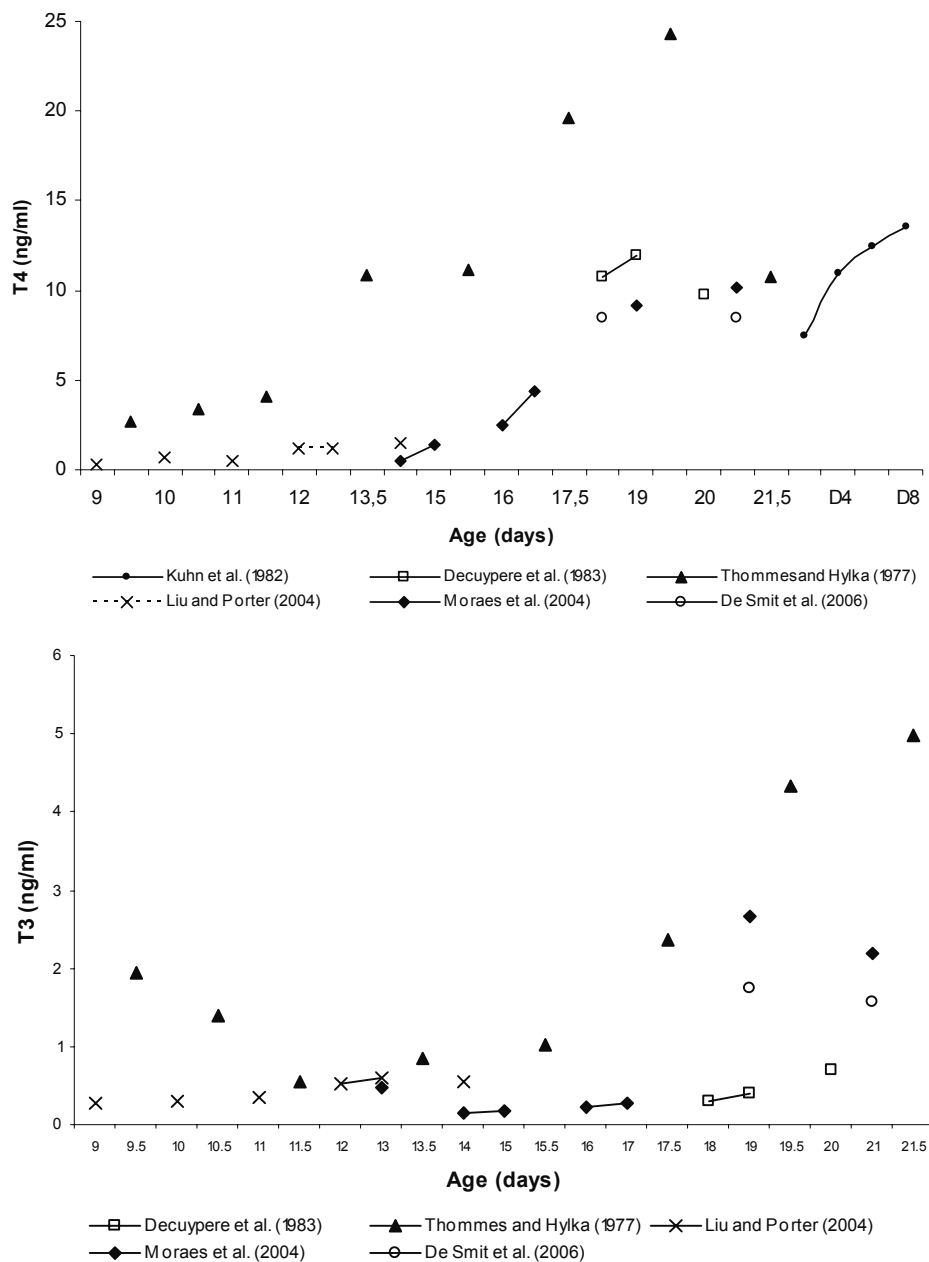


Figure 3 T₄ and T₃ plasma concentrations during embryonic development.

FUNCTIONALITY OF THE AVIAN HYPOTHALAMIC-PITUITARY-THYROID AXIS

In order to evaluate the functional capabilities of the pituitary in relation to thyroid activity, Maraud *et al.* (1983) implanted the adenohypophysis from an 11-day-old chicken embryo into the extra-embryonic coelom of a 3-day-old recipient. The

adenohypophysis strongly influenced the development of the thyroid gland in the 3-day-old embryo by an increased volume of the gland and an increased percentage of colloid and radio-iodide from day 10 of incubation. By day 16 of incubation the values returned to normal in spite of the presence of the additional pituitary. The authors suggested that the adenohypophysis acts autonomously during the early embryonic period, whereas during the last third of embryonic life, the adenohypophysis needs the regulating factor of the hypothalamus.

Synthetic TRH significantly increased plasma T₄ concentrations in 6.5- and 13.5-day-old chicken embryos 3 hours after administration compared with saline-treated individuals (Thommes and Hylka, 1977). The T₄ response to synthetic TRH was stronger in the older embryos (1.71 ng/ml versus 9.81 ng/ml). It seems that the pituitary is able to react to its tropic hormones during the mid-embryonic period, but becomes more sensitive to TRH during the late embryonic period.

The difference in T₄ levels between hypophysectomised and intact chicken embryos from ED11.5 indicates that normal thyroidal activity is autonomously regulated early in embryonic life and becomes 'pituitary dependent' at approximately ED11.5 (Thommes and Hylka, 1977). In common with the pituitary, the thyroid gland is able to react to its tropic hormones during the mid-embryonic period, but becomes more sensitive to those hormones at the end of the embryonic period.

McNichols and McNabb (1988) demonstrated that serum T₄ concentrations showed no increase during TSH stimulation on day 8, 9 and 10 of the incubation period (14-16 days) in altricial ring doves. However, during the post-hatch period, nestlings of all tested ages (2- to 14-day-old) responded to TSH injections by corresponding increases in plasma T₄ concentrations. These data indicate that in the altricial dove, in contrast to the precocial chicken, the pituitary is not functional during the embryonic life and has no influence on the thyroid activity during this period.

Involvement of HPT-axis in avian thermoregulation

INVOLVEMENT OF T₃ AND T₄ IN AVIAN THERMOREGULATION

Freeman (1964) studied the emergence of homeothermy in *Gallus domesticus* by measuring the oxygen consumption of late-term embryos and newly hatched chicks after reducing the environmental temperature from 37.7°C to 30°C. It was clear that the chick was first able to give a sustained metabolic response to a lowered environmental temperature at the moment it escaped from the shell membranes. Freeman (1964) assumed that the thyroid gland plays an important role in the thermoregulatory mechanism of the newly hatched chick. T₃ and T₄, injected peritoneally at a dose of 300 µg/kg in one-day-old chicks exposed to cold (20°C), were equally effective in reducing the rate at which rectal temperature fell in comparison with non-injected chicks (Freeman, 1970). The author concluded that both hormones were thermogenic stimulants.

Tazawa *et al.* (2001) suggested that the development of thermoregulatory abilities in the prenatal and postnatal period of avian species may be attributed to thyroid development. The exact cellular mechanisms of thyroid regulation of thermogenesis are still unclear. Metabolism is mediated by thyroid hormones by their stimulation of mitochondrial oxygen consumption and production of ATP and thereby regulation of basal metabolic rate (BMR), also referred to as obligatory thermogenesis (Bartha, 1993). At day 14 post hatch, the adult follicle cell height of the thyroid gland is reached in precocial birds. The period of increase in follicle cell height coincides with the period of major increase in cooling resistance of young quail (Spiers *et al.*, 1974).

Takahashi *et al.* (2005) found no effect on rectal temperatures with intra-peritoneal injection of T₃ or T₄ (0, 250, 500 and 1000 µg/kg, 8 treatments) in 2-day-old chicks. In 7- and 14-day-old chickens that were injected intraperitoneally on a daily basis with 15µg per 100g bodyweight for 5 days, thyroid hormones increased heat production (Hwang-Bo *et al.*, 1990a). The same was seen in 40-day-old chickens given an intraperitoneal injection of T₃ or T₄ (500 or 1000 µg/kg body weight) (Hwang-Bo *et al.*, 1990b). The thermogenic effect of T₃ administration was greater in week 2 than in week 1 of age (Hwang-Bo *et al.*, 1990a). Muramatsu *et al.* (1986) (cited in Hwang-Bo *et al.*, 1990b) also reported increased heat production in chicks aged 2 to 5 weeks following injection of T₃, but little or no change in heat production was detected in birds at 1 week of age. It seems that enhancing thyroid levels by exogenous injection helps the very young birds to cope under cold stimulation. Under normal temperature, however, the injections seem to have only an effect in older birds.

It was suggested that the failure of exogenous T₃ to stimulate thermogenesis at 1 week of age was due to the hormone-binding sites of receptors being saturated due to either overproduction of T₃, or to poor availability of receptors, or to both (Muramatsu *et al.*, 1986, cited in Hwang-Bo *et al.*, 1990b). When T₃ is produced endogenously in considerable larger amounts than that required to form the hormone-receptor complex, it is clear that no response to exogenous T₃ can be expected. However, when blocking the conversion from T₄ to T₃ by iopanoic acid, rectal temperatures decreased in day-old chicks suggesting a possible role for T₃ in the emergence of thermoregulation (Decuypere *et al.*, 1981).

Borges *et al.* (1980) found that the peripheral conversion of T₄ to T₃ was remarkably increased after hatching. In addition, the level of plasma thyroid hormones was highest at week 1 of age (Davison, 1976). These findings support the hypothesis of the possible saturation on the hormone-receptor sites. Edelman and Ismail-Beigi (1974), however, suggested that the unresponsiveness to T₃ administration could be brought about by incomplete function of the subsequent reactions that are responsible for T₃-sensitive heat production systems, such as Na⁺, K⁺-adenosine 5'-triphosphatase. Additionally, Takahashi *et al.* (2005) suggested that the relatively small muscle mass of neonatal chicks may explain the lack of effects of thyroid hormones on body temperature.

Although there is a clear effect of T₃ and T₄ on the heat production in chicks of 2 weeks old, the reason for a lack of response to changed concentrations of T₃ in younger chicks under normal temperature is still not obvious. It is possible that the T₃-sensitive heat production systems are still immature in the first week post hatching, but this hypothesis needs further investigation.

DIRECT INVOLVEMENT OF TRH IN AVIAN THERMOREGULATION

TRH is not only known as a hypothalamic signal to the HPT-axis, but also appears to act in thermoregulation in mammals (Metcalf, 1974). Lin *et al.* (1980) found that intracerebroventricular (ICV) injection of TRH altered heat production (HP) in rats demonstrating that central TRH is involved in the regulation of energy expenditure in mammals. ICV injection of TRH in neonatal chicks induced hyperthermia and increased body temperature in a dose-dependent way (Takahashi *et al.*, 2005) and significantly increased O₂ consumption and CO₂ production in 2-day-old chicks (Tachibana *et al.*, 2006). In an older study, Nisticò *et al.* (1978) already demonstrated that TRH (ICV injection) increased the respiratory rate and locomotion activity in chicks.

However, thyroid hormone levels were not stimulated by this injection of TRH (Takahashi *et al.*, 2005). Furthermore, peripherally administered thyroid hormones did not enhance body temperature suggesting that the effect of ICV injected TRH is not related to thyroid hormones (Takahashi *et al.*, 2005). These facts lead to the hypothesis

that TRH itself is involved in the regulation of energy expenditure in chicks, and is not acting in altered thyroid hormone levels. A different way of administration (intravenous injection of TRH in 1-day-old chicks), however, led to increases in T₃ and T₄ (Decuypere *et al.*, 1988). Because CRH seems to induce thermogenesis in neonatal chicks (Tachibana *et al.*, 2004), Tachibana *et al.* (2006) investigated whether the effect of an ICV injection of TRH on the thermoregulation in chicks was CRH mediated (since it was clearly T₃ and T₄ independent). However, they had to conclude that in the brain, TRH increased heat production via CRH-independent mechanisms. The mechanisms involved in the TRH-induced increase in heat production need to be clarified in the future.

Interaction of the HPT-axis with the HPA-axis in ontogeny of thermoregulation

Many central factors influence the regulation of energy homeostasis and have been shown to be vital in thermogenesis and metabolism. CRH rapidly mobilizes the organism for responses to stressors and also stimulates the central nervous system to respond to environmental changes (Carlin *et al.*, 2006). ICV infusion of CRH is shown to increase brown adipose tissue thermogenesis in rats (Rivest *et al.*, 1989) and even increases whole body oxygen consumption and colonic temperatures (De Fanti and Martinez, 2002).

Tachibana *et al.* (2004) found that ICV injection of 100 ng CRH induced thermogenesis in neonatal chicks (4-day-old). Rectal temperature was significantly increased at all times measured (10, 30 and 60 minutes after injection). In a subsequent study it was found that ICV injection of 2.1 or 21 pmol CRH increased O₂ consumption and CO₂ production in a significant way in 2-day-old chicks as well as heat production (Tachibana *et al.*, 2006).

Although TRH is considered to be the main regulator of TSH secretion within the HPT-axis, several other hypothalamic factors like CRH and somatostatin (SRIH) are known to influence TSH release in the chicken. Neural elements, reacting with antibodies generated against synthetic ovine corticotropin releasing factor (CRF), were first detected in perikarya located in the periventricular part of the hypothalamus on the 14th day of the incubation period of the chicken embryo (Józsa *et al.*, 1986). Meeuwis *et al.* (1989) showed that injection of several doses (0.5, 1, 2, and 5 µg) of ovine CRH (oCRH) increased not only plasma corticosterone levels, but also circulating T₄ and T₃ concentrations in 18-day-old chicken embryos. Geris *et al.* (1996) found that TSH is involved in this CRH effect on thyroid function, because they observed a rapid elevation of TSH plasma levels after oCRH administration. oCRH, however, did not influence the secretion of T₄ by isolated thyroid glands *in vitro*. Therefore, it seems obvious that CRH is a potent TSH-releasing factor in the chicken. Thyrotrophs were shown to be already responsive to CRH stimulation at the first age tested by Geris *et al.* (2003), *i.e.* ED14, and they seem to remain so throughout the entire life cycle of the chicken. The authors observed that both TRH and CRH become less effective in increasing circulating TSH levels in adult chicken. De Groef *et al.* (2003) found that thyrotrophs express chicken CRH-receptor 2, but only few chicken CRH-receptor 1. This finding implies that CRH-receptor 2 plays a role in the transduction of the CRH stimulus for TSH release.

Conclusions

The interdependence of the HPT-axis occurs towards the end of incubation in precocial

birds while the axis becomes functional in the first weeks post hatching in the altricial avian species. Thyroid hormones peak prior to hatch in precocial birds, while the highest levels of these hormones occur in the first week post hatching in altricial species.

T₃ and T₄ seem to have thermoregulatory abilities from week 1 post hatching. However, there is little evidence that the thyroid hormones play an important role in the emergence of thermoregulation. A decrease in rectal temperatures was only observed when the conversion from T₄ to T₃ was blocked in day-old chicks, suggesting a possible role for thyroxine in the ontogeny of thermoregulation. The thyroid releasing hormone (TRH) has a major impact on the thermoregulation of younger and older chicks. The exact mechanisms are still unknown and further research is required.

Several investigations indicate that CRH is the main hormone from the HPA-axis which is involved in thermoregulation. There exists a close relationship between the HPT- and the HPA-axis in chickens even as early as ED19.

From both hormonal axes TRH and CRH seem to have the greatest influence on the emergence and the regulation of thermoregulation. This leads to the assumption that hormones, produced by the hypothalamus are possibly more important in thermoregulatory abilities of birds than their end organ products, thyroid and adrenocorticoid hormones, respectively.

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