Endocrinology of thermoregulation in birds in a changing climate

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Abstract

The ability to maintain a (relatively) stable body temperature in a wide range of thermal environments is a unique feature of endotherms such as birds. Endothermy is acquired and regulated via various endocrine and molecular pathways, and ultimately allows wide aerial, aquatic, and terrestrial distribution in variable environments. However, due to our changing climate, birds are faced with potential new challenges for thermoregulation, such as more frequent extreme weather events, lower predictability of climate, and increasing mean temperature. We provide a compact overview on thermoregulation in birds and its endocrine and molecular mechanisms, pinpointing gaps in current knowledge and recent developments, focusing especially on non-model species to understand the generality of, and variation in, mechanisms. We highlight plasticity in thermoregulation and underlying endocrine regulation, because thorough understanding of plasticity is key to predicting responses to changing environmental conditions. To this end, we discuss how changing climate is likely to affect avian thermoregulation and associated endocrine traits, and how the interplay between these physiological processes may play a role in facilitating or constraining adaptation to a changing climate. We conclude that while the general patterns of endocrine regulation of thermogenesis are quite well understood, at least in poultry, the molecular and endocrine mechanisms that regulate e.g. mitochondria function and plasticity of thermoregulation over different time scales (from transgenerational to daily variation) need to be unveiled. Plasticity may ameliorate climate change effects on thermoregulation to some extent, but the increased frequency of extreme weather events, and associated in resource availability, may be beyond the scope and/or speed for plastic responses. This could lead to selection for more tolerant phenotypes, if the underlying physiological traits harbour genetic and individual variation for selection to act on – a key question for future research.

Keywords: avian, thermoregulation, thyroid hormone, corticosterone, NST, avUCP, BMR, plasticity, climate change, temperature, weather, metabolic rate, heterothermy

1. Aims and motivation

Birds maintain a high and (relatively) stable body temperature (T_b), on average 41.02 ± 1.29°C (s.d.) at rest during the active phase (Prinzinger et al., 1991), across a wide range of thermal environments via physiological, morphological and behavioural modifications, including endocrine regulation.. This endotermic lifestyle enables the wide aerial, aquatic, and terrestrial distribution of birds in variable habitats across the globe (Yahav, 2015). For example, desert birds are able to live and reproduce in arid conditions up to +50°C where the environment is hotter than their own bodies, while resident species in temperate regions routinely deal with seasonal variations surpassing 60°C and winter temperatures that may be 80°C below T_b. Due to our changing climate, all organisms, including birds, are faced with potential new challenges for thermoregulation, such as more frequent extreme weather events, lower predictability of climate, and increasing mean temperature (IPCC 2014). The key question is how they will respond and potentially adapt.

The first aim of this review is to provide a compact overview on thermoregulation in birds and its endocrine and molecular mechanisms, pinpointing gaps in current knowledge and recent developments. We especially focus on plasticity in thermoregulation and underlying endocrine mechanisms, because proper understanding of plasticity is a key to predicting responses to changing environmental conditions. Because current literature is biased towards work on poultry, we have put special emphasis on studies in non-model species and wild populations to understand the generality of, and variation in, mechanisms. To our knowledge, there are no previous reviews that tie together the complexity of the endocrine basis of T_b regulation in birds with plasticity of thermoregulation under climate change, whilst also accounting for the latest molecular data. This summary will set the stage for the second set of goals: discussing challenges for avian thermoregulation in the face of climate change, how this may affect endocrine traits, and how these processes combine to facilitate or constrain adaptation to the changing world. We purposely use the wording 'climate change' over 'global warming' throughout, to account for the multitude of direct and indirect changes in the environment that challenge avian thermoregulation.

Box 1. Glossary of key terminology concerning thermoregulation (following IUPS Thermal commission 2003)

Acclimatization physiological or behavioural changes that occur within the lifetime of an organism to reduce the strain of variation in the natural climate in the wild, such as geographic or seasonal responses to variation in ambient temperatures

Basal Metabolic rate (BMR) Metabolic energy transformation calculated from measurements of heat production or oxygen consumption in a rested and awake organism that is within its thermoneutral zone and has fasted sufficiently long to be in a postabsorptive state

Endothermy The pattern of thermoregulation of animals in which the body temperature depends on a high and controlled rate of heat production

Epigenetic temperature adaptation Lifelong(?) thermal adaptation that is triggered during prenatal (embryogenesis) or early posthatching ontogeny, influencing the individuals' capacity to produce or dissipate heat

Hyperthermia The condition of an animal where body core temperature is above its range specified for the normal active state of the species

Hypothermia The condition of an animal where body core temperature is below its range specified for the normal active state of the species

Non-shivering thermogenesis (NST) Heat production due to metabolic energy transformation by processes that do not involve contraction of skeletal muscles

Resting Metabolic Rate (RMR) The metabolic rate of an animal at rest in a specified environmental context, and not necessarily in a postabsorptive state.

Shivering thermogenesis (ST) Heat production due to increased contractile activity of skeletal muscles (not involving voluntary movements)

Thermoneutral zone (TNZ) the range of ambient temperatures at which normothermic body temperature is maintained without regulatory changes in metabolic heat production or heat dissipation

2. A brief overview of thermoregulation in birds

The thermoregulatory system that enables maintenance of a relatively constant T_b over a wide range of environmental temperatures in birds consists of (Fig 1, modified from Yahav, 2015): (1) a *sensory part*, which detects changes in the environment (thermo-, osmo-, and baro-receptors), (2) *an integrating part*, the thermoregulatory center at preoptic anterior hypothalamus (PO/AH), in which temperature-sensitive neurons monitor local temperature changes and temperature information received from peripheral thermoreceptors. The T_b set point is then defended by mechanisms for heat production or heat loss depending on the thermal status of the bird; and (3) *the command part*, involving neurological and endocrine signals that lead to downstream mechanisms for T_b control, viz. shivering thermogenesis (ST), potentially non-shivering thermogenesis (NST), evaporative heat loss (including respiratory- and cutaneous heat loss), peripheral vasoconstriction or vasodilation, and behavioural changes (e.g. basking, huddling, shade/cover seeking). In ST, the birds increase the rate of heat production by increased contractile activity in the skeletal muscles, whereas, in NST, heat production is increased via metabolic energy transformations which do not include contraction of muscles. ST contributes most to thermogenesis in birds (e.g. Hohtola, 2002). NST (in muscle and liver tissue contrast to mammalian brown adipose tissue NST) is probably widespread in birds (e.g. Dridi et al., 2008; Mozo et al., 2005; Raimbault et al., 2001; Talbot et al., 2004; Vianna et al., 2001a; Vianna et al., 2001b), but direct evidence for a significant contribution of NST to heat production is still scarce (Teulier et al., 2010; Teulier et al., 2014). In this review we focus on endocrine mechanisms underlying thermoregulation, while neuronal mechanisms in vertebrates have been reviewed elsewhere (e.g. Morrison et al., 2008).

3. **Endocrine and molecular mechanisms of thermoregulation in birds**

3.1. The role of the hypothalamus-pituitary-thyroid (HPT) axis in avian thermoregulation

Thyroid hormones (THs, triiodothyronine, T3 and thyroxine, T4) are the most important hormones controlling thermogenesis; a link that was established already in the late 1950’s (e.g. Decuypere et al., 2005; Klandorf et al., 1981; Mellen and Wentworth, 1958; Mellen and Wentworth, 1962). The proposed hormonal and molecular pathways with HPT-axis involvement on thermogenesis are outlined in Fig 2.

PO/AH is activated by input from thermoreceptors, which stimulate the hypothalamic paraventricular nucleus (PVN) and leads to an increase in thyrotropin (TRH) synthesis and secretion (Arancibia et al., 1996). TRH stimulates the thyrotrophs in the anterior pituitary to secrete 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 T4) synthesis and release. The secretion of TSH by the pituitary is (besides hypothalamic TRH) modulated by a negative feedback mechanism of T3. Alternatively, cold exposure can lead to increased conversion of T4 to T3 (and less to inactive rT3) by deiodinase enzymes (DIO1-3) in tissues, mostly in the liver (Collin et al., 2003a; Van der Geyten et al., 1999), thus leading to higher circulating T3 levels. In tissues, T3 binds to both nuclear and mitochondrial receptors and influences gene expression to modulate metabolic rates and respiration (see below).

There is experimental evidence supporting the modulatory role of THs on thermoregulation within the TNZ (also coined ‘obligatory thermogenesis’): For example, experiments where birds were made hypothyroid (i.e., lacking THs) using TH blockers, or when thyroid glands were removed (thyroidectomy), reported reduced heat production in poultry (e.g. Mellen and Wentworth, 1962), whereas experimental administration of THs stimulated thermogenesis (Arieli and Berman, 1979). Experimental elevation of THs in blood increased thermogenesis also in non-model species, little buntings (*Emperiza pusilla*) (Liu et al., 2006), and correlations between THs and thermogenesis were observed in goldfinches (*Carduelis tristis*)(Dawson et al., 1992), great tits (*Parus major*) and willow tits (*P. montanus*) (Silverin et al., 1989). In addition, a growing body of (mostly correlational) evidence suggests a positive association between THs and basal metabolic rate (BMR) in several non-model bird species measured in free-ranging populations (Bobek et al., 1977; Chastel et al., 2003; Kim, 2008; Liu et al., 2006; Vezina et al., 2009; Zheng et al., 2014a).

Thyroid hormones are also important for thermogenesis below thermoneutrality (also coined ‘facultative thermogenesis’ see Fig 2). Potential mechanisms for elevating the capacity for thermogenesis in birds include (i) increasing muscle mass devoted to ST and possibly NST (but see Milbergue et al., 2018 for recent contrasting results) (ii) increasing mass–specific aerobic enzyme capacity of muscle tissue (Bicudo et al., 2002; Liknes and Swanson, 1996; potentially also liver, see Liu et al., 2006), and (iii) increasing mitochondrial density and/or respiration rate to fuel aerobic metabolism, and (iv) possibly increased capacity to uncouple mitochondria from energy production, causing energy that would have been used to phosphorylate ADP to ATP to be released as heat (Collin et al., 2003b; Dridi et al., 2004). Thyroid hormones are likely involved in regulating NST, while ST may be predominantly controlled directly via neuronal mechanisms (Morrison et al., 2008).

The molecular mechanisms of NST (and even its existence, see Hohtola 2002) in birds have been heavily discussed but as there seems to be no clear consensus (e.g. Dridi et al., 2004; Walter and Seebacher, 2009), we briefly review the potential pathways. One of the potential molecular mediators of NST is the avian homolog of mammalian uncoupling protein (avUCP) - an anion-carrier protein that, by dissipating the proton gradient across the inner mitochondrial membrane, potentially uncouples respiration from ATP synthesis. avUCP expression was first described in muscle tissue in Muscovy ducklings (*Cairina moschata*) and swallow-tailed hummingbirds (*Eupetomena macroura*) (Raimbault et al., 2001; Vianna et al., 2001b). The potential role of avUCP in NST is supported by its increased expression in cold-exposed, and decreased in heat-exposed, birds (chicken and king penguin, *Aptenodytes patagonicus)* (Dridi et al., 2008; Mozo et al., 2005; Raimbault et al., 2001; Talbot et al., 2004; Vianna et al., 2001a; Vianna et al., 2001b). An increase in avUCP expression was associated with increased plasma T3 levels and heat production in chicken (Collin et al., 2003a). Furthermore, THs caused an overexpression, while a thyroid blocker (methimazole) treatment significantly downregulated the expression of avUCP-mRNA (Collin et al., 2003b; Walter and Seebacher, 2009), supporting the involvement of THs in avUCP regulation. However, experimentally increased metabolic heat production occurred in parallel with an upregulation of avUCP in Muscovy ducklings, but the increased expression of avUCP was not associated with coupling of ATP production to oxygen consumption (Teulier et al., 2010). Furthermore, Walter and Seebacher (2009) showed that blocking adenine nucleotide translocase (ANT), but not avUCP, significantly reduced muscle and liver mitochondrial uncoupled respiration rates, suggesting that instead of avUCP, ANT would be the principal uncoupling protein in birds. ANT may also be controlled by THs, because its expression was decreased by TH blockers (Walter and Seebacher, 2009). In turn, avUCPs could have other functions, for example as modulators of reactive oxygen species (ROS) production (Rey et al., 2010).

Another putative mechanism for NST involves Ca2+ slippage controlled by the peptide sarcolipin (SLN), which has been characterized in mammals (reviewed in Nowack et al., 2017). In this pathway, NST in muscle cells is activated by the binding of the SLN to the Ca2+ ATPase (SERCA), which is the transmembrane Ca2+ pump located in the sarcoplasmic reticulum (SR) membrane. SLN causes Ca2+-slippage with the sole purpose of heat generation. In birds, there is a profound increase in SERCA activity during cold exposure (Dumonteil et al., 1995) and prolonged cold exposure also leads to increase in the Ca2+ channels through which Ca2+ is normally released from the SR (ryanodine receptors) (Dumonteil et al., 1995). Thus, it seems that the mechanism of muscle NST in birds could also involve ATP hydrolysis by SERCA. However, presently it is not known if SNL is involved in heat production in this taxon, and if THs are involved in the SERCA pathway, as in mammals (Silva, 2006). Finally, THs also influenced expression of PGC1, a known metabolic mediator in mammals (Walter and Seebacher, 2007; Walter and Seebacher, 2009), providing another potential molecular mediator for thermogenesis in birds.

Mitochondria in avian skeletal muscle have been recently found to express TH receptors (Lassiter et al., 2018), which supports the role of THs in regulation of mitochondrial function (see e.g.Cioffi et al., 2013 for reviews on mammals; Lanni et al., 2016). However, the exact molecular mechanisms how THs may be controlling e.g. ANT or SERCA and thus NST in birds are not understood, while in mammals, UCP and PGC1 sequences show response elements for thyroid hormone receptor (e.g. Rabelo et al., 1996; Wulf et al., 2008). Also non-genetic pathways of TH action have been characterized, mostly in rodents (reviewed in Cheng et al., 2010; Davis et al., 2016; Davis et al., 2018; Singh et al., 2018), while some indication of non-genomic influence of THs on mitochondria e.g. glucose update was observed in chicken embryos (Segal and Gordon, 1977).

In most studies, associations between THs and thermogenesis are based on circulating TH measurements. However, the final availability of THs is influenced by plasma binding proteins, conversion of THs by deiodinase enzymes (DIO1-3) in the target tissues, and the responsiveness to THs depends on receptor densities (Darras et al., 2006). As expected, ambient temperature has also been found to influence deiodination: Increased hepatic T4 to T3 conversion via increased DIO2 expression was detected in cold-exposed chickens (Ikegami et al., 2015; Rudas and Pethes, 1984; Rudas and Pethes, 1986), while heat stress decreased DIO2 expression (Jastrebski et al., 2017). Cold exposure also decreased hepatic DIO3 activity in chicks (Collin et al., 2003a), leading to less T3 degradation. While TH receptors have been identified in mitochondria (Lassiter et al., 2018), to our knowledge, variation in TH receptor expression (either nuclear or mitochondrial) has not been studied in response to temperature variation in birds. In mice and rats, mitochondrial receptor (p43) overexpression was recently found to be associated with higher T_b (Bertrand-Gaday et al., 2016). In vivo (knockout) and in vitro studies in mice revealed that p43 is associated with mitochondrial biogenesis, activity, mito-nuclear crosstalk and even muscle metabolic and contractive phenotype (reviewed in Wrutniak-Cabello et al., 2017; Wrutniak-Cabello et al., 2018), but similar data is lacking from birds.

3.2. The role of the hypothalamus-pituitary-adrenal (HPA) axis in avian thermoregulation

Corticosterone (CORT) is the avian glucocorticoid hormone. Glucocorticoids are crucial for maintaining physiological and energetic homeostasis: Following a stressor CORT is released from the adrenals in response to adrenocorticotropic hormone (ACTH) from the hypothalamus. Fast temperature changes, induced by both cooling and heating, have been shown to increase circulating CORT across captive and wild species in both correlative and experimental studies (Bize et al., 2010; de Bruijn and Romero, 2011; Frigerio et al., 2004; Jessop et al., 2016; Jimeno et al., 2018; Krause et al., 2016; Wingfield, 2015; Wingfield et al., 2017; Xie et al., 2017); Shipley et al. 2019). Thus, it has been suggested that CORT may play a role in responding and adapting to rapid temperature changes. Despite repeated observations of such patterns, the exact mechanism for how CORT may be linked to thermoregulation, either physiologically or behaviourally, is not well understood. Because CORT is needed for the synthesis of glucose from liver glycogen or fat reserves, the most likely explanation is that this hormone mobilises internal energy reserves, and/or activates food searching behaviour to fuel the higher metabolic rate in cold conditions (de Bruijn and Romero, 2011; Jimeno et al., 2018). Mitochondrial glucocorticoid receptors have recently been detected in avian muscle cells, which suggests that CORT may also play a role in regulating mitochondrial function and, hence, energy production (Lassiter et al., 2018). Recent transcriptomic and metabolomic studies may shed light on the potential pathways. For example, under heat stress both glycogenolysis and gluconeogenesis pathways are elevated in the liver, providing endogenous energy sources under stress (Jastrebski et al., 2017). Finally, recent correlative studies also suggest an association between baseline CORT, peripheral body temperature, and slow changes in environmental temperature over winter and summer (blue tits, Jerem et al., 2018), which may indicate that CORT is not only involved in short-term heat/cold stress.

In addition to its potential role in responses to thermal stress, the HPA-axis is likely to also play a role in the ontogeny of avian thermoregulation, interacting with the HPT-axis (reviewed in Debonne et al., 2008). In particular, corticotropin releasing hormone (CRH) is involved in thermoregulation: in neonatal chicks, injection of CRH induced thermogenesis and increased T_b (Tachibana et al., 2004; Takahashi et al., 2005). CRH injection in chicken embryos also increased TSH and circulating T4 and T3 concentrations (Meeuwis et al., 1989), suggesting interactions between CRH and THs on thermoregulation. In support of CRH-mediating effects via THs (on thermoregulation), chicken thyrotrophs were found to express CRH-receptor 2 (De Groef et al., 2005). Interestingly, the HPT-axis became less responsive to CRH in adult chickens (Geris et al., 2003), likely due to altered interaction with the peripheral TH deiodinase enzymes (Darras et al., 2006), thus showing that such interactions between hormones on thermoregulation may vary across stages in ontogeny.

3.3. The role of potential other endocrine mechanisms in thermoregulation

There is a plethora of other neuropeptides and hormones that may be linked to thermoregulation, but the role of these is largely unexplored, especially beyond chicken models. It is also well understood that many hormonal axes are likely to interact (see also above). Nguyen et al. (2015) discovered that hypothalamic orexigenic *neuropeptide Y* (NPY) responds to cold exposure in poultry. *Melatonin*, an indoleamine produced in the pineal gland, has been implicated to play a role in avian thermal homeostasis (John and George, 1991). Experimental melatonin administration increased T_b in chickens (e.g. Sinkalu et al., 2015), and induced improved cold resistance, thermal insulation and maximal heat production (similar to cold acclimatization) in quails (Saarela and Heldmaier, 1987; Saarela and Reiter, 1994). This is in line with melatonin showing seasonal and circadian patters, and thus conveying information on seasonal progression in birds and mammals (Nelson and Demas, 1997; Reierth et al., 1999).

Balancing energetic needs is essential for thermoregulation: both ST and NST, and (some routes of) evaporative heat loss require energy, the availability of which often fluctuates with high/low environmental temperatures. A few key hormones are likely to be involved with energy balance during thermal stress: *Leptin* was found to be elevated following acute heat and cold stress in liver and plasma in chicken (Dridi et al., 2008). It has been suggested to be involved in regulating feed intake and lipid metabolism (reviewed in Zhang 2018), which are tightly linked with thermoregulation. *Ghrelin*, a peptide hormone produced mainly in the gastrointestinal tract, may also be indirectly linked to thermoregulation: peripheral administration of ghrelin in turkeys increased levels of plasma CORT, glucose and T4 (Shahryar and Lotfi, 2017), suggesting indirect effects via e.g. thyroid hormones. Moreover, experimentally increased leptin and ghrelin was associated with mass gain in the coal tit (*Periparus ater*, Henderson et al., 2018), which is likely to also (indirectly) influence thermoregulation during winter.

In hot and dry environments, thermoregulation is often directed towards heat dissipation which is mostly achieved by evaporative cooling. Because this is costly in terms of water (Nord and Williams, 2015; Tieleman and Williams, 1999), it is important to understand endocrine regulation of water balance. One of the key regulators is *arginine* *vasotocin* (AVT), produced in the posterior pituitary gland (neurohypophysis) of the brain. Nephew et al. (2005) showed in a series of experiments on starlings (*Sturnus vulgaris*) that peripheral AVT can decrease heart rate, feeding, drinking, preening, and overall activity. AVT also reduced shivering and T_b but had no effects on blood pressure, heart rate or respiratory rate in pigeons (*Columba livia*) (Hassinen et al., 1994; Hassinen et al., 1999). Finally, AVT was further found to increase plasma levels of T4, and a decrease in that of T3 (John and George, 1992), which may be one of the mechanisms linking AVT to thermoregulation.

3.4.Conclusions and notes

The majority of the known endocrine mechanisms in thermoregulation concern thermogenesis, i.e. the production of heat below the TNZ. However, it is equally important to understand the endocrine and neurological mechanisms of thermoregulation above the TNZ where heat needs to be dissipated to keep T_b at set point and prevent overheating. These include evaporative heat loss, facultative hyperthermia, vasodilation and multiple behavioural responses, such as seeking cooler microclimates. Heat loss, vasomotor action, as well as many of the behavioural effects are likely under neuronal control, including dopamine, as suggested in mammals (Madden and Morrison, 2019; Terrien et al., 2011). However, there are few corresponding data for birds. Filling these knowledge gaps can be important to understand responses to climate-change driven extreme weather, such as heat waves and droughts, which is expected to become more frequent in the coming years (see section §5).

Furthermore, as thermoregulation is dependent on energy (in cold environments) and water (in hot environments) balance, the associated endocrine pathways of water and energy intake should also be considered for a more complete understanding of the physiological state. Thus, the relative contributions of other hormonal controllers of organismal thermal biology beyond HPT and HPA axis on thermoregulation need to be further clarified.

4. Plasticity in thermoregulation and its endocrine control – five time-scales

Many bird species have a large capacity to plastically respond to varying environmental temperature on different time scales via: (i) rapid stress-induced hyperthermia (ii) short-term facultative hypo- or hyperthermia (iii) acclimatization, (iv) epigenetic temperature adaptation or (v) transgenerational plasticity, as summarised in Fig 3.

4.1. Rapid stress-induced hyperthermia

Birds, like other endotherms, respond to acute ecological and psychological stressors (e.g. predation) via stress-induced hyperthermia (Cannon, 1915). The response is triggered immediately upon exposure to the stressor, and reflects increased T_b set point regulated by the sympathetic-adrenal-medullary pathway, while CORT could also play some role (Briese and Cabanac, 1991; Yahav, 2015). For certain stimuli, the thermoregulatory changes during stress are sensitive to variation in environmental temperature (Nord and Folkow, 2019). However, because stress-induced hyperthermia predisposes the bird for flight-or-fight behaviour to increase short-term/immediate survival, it is unlikely that this will be significantly altered in a climate change context, so these responses will not be discussed further.

4.2. Facultative hypo- and hyperthermia

T_b of birds fluctuates substantially around the normothermic mean (41.02 ± 1.29°C (s.d.)) during the circadian cycle, on average being 2.9°C higher during strenuous activity and 2.5°C lower during rest at night with larger daily amplitude in smaller species (Prinzinger et al., 1991). Many bird species deviate even further from normothermia over time periods ranging from *a few hours to several days* (reviewed in Gerson et al., 2019) (McKechnie and Lovegrove, 2002; Ruf and Geiser, 2015), which is referred to as facultative hypo- and hyperthermia.

Birds that are energy limited, either because they feed on ephemeral resources, have high energy turnover rates, or reside in challenging (e.g. resource-poor, cold) environments, frequently employ facultative hypothermia, i.e. a reduction in T_b below normothermia (McKechnie and Lovegrove, 2002). This reduces the need for thermogenesis because heat is lost at slower rate when the gradient between the animal and the environment is lessened, and also reduces maintenance metabolic rate as colder tissues consume less energy. Facultative hypothermia is therefore often interpreted as an adaptation to counter unpredictable food availability and/or increased energetic needs during both winter and breeding season (McKechnie and Lovegrove, 2002; Nilsson and Nord, 2017; Ruf and Geiser, 2015), and might sometimes also be used to facilitate fuel loading rate in migratory birds on stopover (Wojciechowski and Pinshow, 2009) This strategy is employed widely across the avian phylogeny (McKechnie and Lovegrove, 2002). However, the magnitude of the reduction in T_b ranges from a few degrees of ambient lasting several hours or days, in e.g. nightjars and hummingbirds, to the rather shallow hypothermia ≤ 10°C of normothermia that seems to be prevailing in many northern passerines (McKechnie and Lovegrove, 2002). The common poor-will (*Phalaenoptilus nuttalli*) even remains in a hypothermic state for weeks, reminiscent of hibernation in mammals (Jaeger, 1949a; Jaeger, 1949b). It is clear that deeper hypothermia confers greater energy savings, but also comparatively moderate reduction of energy expenditure during shallow hypothermia can come with significant fitness benefits (Brodin et al., 2017).

In hot and dry climates, birds frequently use facultative hyperthermia, i.e., regulating T_b above the normal level. This reduces the need for evaporative cooling, and hence demand for water, for at least three reasons (reviewed by Gerson et al., 2019). Specifically, by reducing the gradient between T_b and ambient temperature, the bird gains less heat from the environment and (when T_b is higher than ambient) will also be able to lose some heat passively by 'dry' heat loss (i.e., radiation, convection, conduction). This reduces the need for evaporative cooling. Also, by allowing T_b to increase, the bird stores heat inside the body that can be dissipated non-evaporatively outside the hottest hours of the day when the body is again colder than the environment. For example, incubating greater hoopoe larks (*Alaemon alaudipes*) in a desert environment of 40°C would save 15-20% of total evaporative water loss by heat storage alone when they let T_b increase from 42°C to 45°C (Nord and Williams, 2015). Use of facultative hyperthermia is widespread especially amongst desert dwellers, though mechanisms involved and capacity for evaporative cooling varies with body mass and phylogeny (Gerson et al., 2019).

The molecular and endocrinological mechanisms underlying facultative hypo- and hyperthermia are not well understood. CORT could play a role in regulating facultative hypothermia: in hummingbirds external CORT increased the use of torpor (Hiebert et al., 2000). In mammals, experimental administration of testosterone has been shown to inhibit torpor (Mzilikazi and Lovegrove, 2002). This could also explain why, in birds, torpor was restricted to females in the Puerto Rican tody (*Todus mexicanus*) (Merola-Zwartjes and Ligon, 2000), and hypothermia was deeper in females compared to males in Eurasian skylarks (*Alauda arvensis*) and blue tits (Nord et al., 2009; Powolny et al., 2016). Finally, in chicken models, low temperature combined with fasting, suppressed hepatic DIO2 and serum

T3 level (Ikegami et al., 2015), which suggest that THs may also function as a regulatory mechanism for facultative hypothermia in cold and food-restricted conditions.

4.3. Acclimatization

Acclimatization of thermoregulation refers to reversible physiological or behavioural changes that occur within the lifetime of an organism to allow the individual to cope with longer-term temperature variation *over days or weeks*. This allows maintained performance over a range of environmental conditions, such as between seasons and across the species' distribution range among populations (Fig 3). There is evidence that THs play a role in seasonal acclimatization: For example, in wild migratory birds such as white-crowned sparrows (*Zonotrichia leucophrys*) and red knots (*Calidris canutus canutus*), annual cycles of THs are correlated with seasonal changes in BMR, suggesting that seasonal changes in TH could be involved in adjusting energy expenditure to environmental conditions (Jenni-Eiermann et al., 2002). In resident birds, passerines showed enhanced thermogenic capacities via seasonal increases of muscle tissue used for thermogenesis (mainly the pectoral muscle in flying birds, also leg muscles in Galliformes and Anseriformes, reviewed by Hohtola, 2002) and growth of metabolically active organs such as the liver and heart (reviewed by Swanson and Vezina, 2015). These changes were coupled to increased activity of respiratory enzymes and higher levels of T3 (Burger and Denver, 2002; Liknes and Swanson, 2011a; Liknes and Swanson, 2011b; Silverin et al., 1989; Smit and McKechnie, 2010; Zheng et al., 2014a; Zheng et al., 2014b), supporting the role of THs in seasonal acclimatization.

4.4. Epigenetic adaptation

Epigenetic temperature adaptation (e.g. Yahav, 2015) means that exposure to temperature variation during the ontogeny of the thermoregulatory system (and HPT- and HPA-axes) alters thermal physiology, which influences the capacity of the individual to respond to variation in thermal environment in early and later life. In broader terms, this phenomenon could be classified under developmental plasticity/programming (e.g. Stearns, 1989). Thermal environment during development has been suggested to play a role in determination of the set point for physiological control systems (Piestun et al., 2009; Tzschentke and Basta, 2002). For example, chickens that are cold-exposed in the egg are better heat-producers before and after hatching, and also later in life. In contrast, pre-natal heat exposure to heat challenges cope better in higher ambient temperatures later in life (Kamanli et al., 2015; Loyau et al., 2015; Morita et al., 2016; Piestun et al., 2009; Piestun et al., 2008a; Piestun et al., 2008b; Piestun et al., 2015). For non-domesticated species, Nord & Nilsson (2011) and DuRant et al. (2011), found that blue tits and wood ducks (*Aix sponsa*) that were cold-incubated had higher metabolic rate close to independence, which was interpreted in the same way – i.e. a response to improve heat production capacity. Altered temperature tolerance is assumed to be associated with altered HPT-axis function, as chickens that were exposed to pre-natal heat showed reduced TH levels and altered deiodinase enzyme expression in response to a thermal challenge later in life (Loyau et al., 2014; Nassar et al., 2015; Piestun et al., 2009; Piestun et al., 2008a; Piestun et al., 2008b). In wood ducks, thermal manipulation also influenced TH levels in hatchings (altough later life THs nor responses to thermal stress were not studied, DuRant et al., 2014), suggesting the role of HPT-axis involvement in epigenetic adaptation across avian species. Interestingly, heat exposure also altered stress-induced CORT later in life (e.g. Wilsterman et al., 2015). Thermal manipulation affected the proportion of thermosensitive neurons, which can then influence the downstream neuronal and hormonal responses involved in thermoregulation (Loh et al., 2004; Tzschentke and

Basta, 2002). At the cellular level, expression of heat shock proteins (HSPs, i.e. protective protein chaperones) was lower in birds that were heat-challenged in the egg compared to controls when chicks were exposed to a thermal challenge after hatching. Interestingly, this was accompanied with altered DNA methylation of the HSP promotor regions (Vinoth et al., 2018). Recent transcriptomic studies suggest that pre-natal heat exposure may further affect vascularization and angiogenesis in the chicken, likely influencing their ability to thermoregulate (Loyau et al., 2013; Loyau et al., 2016). The neuronal/endocrinological pathways involved in these responses have, however, not been studied. Importantly, it is currently also not understood how permanent such adaptations are, as studies in chicken hardly extend beyond 30 days. This is an interesting avenue for future research, particularly the role of DNA methylation as a potential candidate for long-lasting effects on temperature tolerance.

Most studies have focused on the thermal environment during incubation. However, it is not immediately apparent how changing temperature will affect incubation temperatures in the wild, because parental incubation (the norm in most species) should shelter eggs from substantial temperature fluctuations. Hence, pre-natal temperature would be directly affected by environmental temperature only during the comparatively short period that the nest is unattended. However, both nest attendance and egg temperature during steady-state incubation are also sensitive to variation in weather conditions (Ardia et al., 2009; Ardia et al., 2010; Coe et al., 2015; Nord et al., 2010) suggesting that the combined direct and indirect effects of temperature could significantly affect the pre-natal environment. Even so, we believe that an important avenue for further research will be to also address if post-hatching temperature could also have similar developmental programming functions, because chicks are arguably poorly buffered against temperature variation before their thermoregulatory system fully develops~~.~~ For example, pigeons raised in very hot ambient temperatures in early life were found to have improved capacity for evaporative cooling as adults (Marder and Arieli, 1988). A handful of studies in chicken showed similar effects (Loyau et al., 2015). Birds differ in the timing of development of thermoregulation and maturation of the HPT-axis: in altricial species development occurs post-hatch, while in precocial species it occurs largely during the embryonic period (reviewed by Debonne et al., 2008; McNabb, 2007; Price and Dzialowski, 2018). This suggests that altricial species might be particularly susceptible to epigenetic thermal adaptation post-hatching. Here again, studies extending beyond captive models, such as the precocial chicken, has high potential to reveal important pathways present in other bird taxa.

4.5. Transgenerational plasticity

Ambient temperature variation in the parental environment may also influence offspring thermoregulation and temperature tolerance, so called transgenerational plasticity, as shown recently in multiple taxa (Drosophila: Cavieres et al., 2019; fish: Donelson et al., 2012; reviewed in Donelson et al., 2018; marine invertebrates: Morley et al., 2017; terrestrial invertebrates: Zizzari and Ellers, 2014). Similar data from birds are lacking. However, in birds, low ambient temperature increased the transfer of THs to eggs in great tits (Ruuskanen et al., 2016c), which may have consequences for development (Hsu et al., 2017; Ruuskanen et al., 2016a; Ruuskanen and Hsu, 2018), later HPT-axis function (Hsu et al., 2017), and thus potentially also thermoregulation. Furthermore, in chicken, maternal heat stress influenced embryonic HSP expression and caused global DNA hypomethylation, but also increased oxidative damage (Zhu et al., 2017), while any corresponding influence on thermoregulation and adaptive plasticity has not been studied. Transgenerational plasticity could include a multitude of mediators of parental temperature effects, such as DNA methylation/histone modification, transfer of (small)mRNAs, hormones and other components in the eggs and sperm, with possible links to (the development of) thermoregulation, as shown in other taxa (Adrian-Kalchhauser et al., 2018; Kekalainen et al., 2018; Salinas and Munch, 2012; Weyrich et al., 2016a; Weyrich et al., 2016b).

5. **Thermoregulation in a changing climate**

5.1 What is changing, and what are the challenges for thermoregulation?

Climate change brings about various types of challenges for thermoregulation, the most important of which are summarized in Fig 4. It is likely that the predicted *average* increase of some 1.5°C compared to pre-industrial times by the end of the 21st century will pose, at most, a minor direct threat as both the absolute increase and the slow rate of temperature change is arguably well within scope of short- and long-term adaptations (see plasticity, section §4). Even the predicted maximum increase of 4°C (IPCC, 2014) might not cause immediate threats to most birds, when considering the vast ranges in ambient temperature that are part of daily life for many species, and that even under the worst case scenario yearly temperature change is < +0.1°C. However, we caution on concluding on general trends, first, because the changes in temperature are not likely to be uniform across the globe, e.g. warming is faster in the arctic region , and second, because the scope for further adaptation may be limited in some species, e.g. in desert dwellers that already endure considerable heat load (cf. DuRant et al. 2019).

What is likely to be a more relevant challenge for thermoregulation is the predicted increases in the frequency of weather irregularities, such as heat waves (IPCC, 2014; Rahmstorf and Coumou, 2011; Stillman, 2019; Wingfield et al., 2017), which can bring negative and even lethal consequences in wild bird populations (desert populations of birds Gardner et al., 2017; McKechnie and Wolf, 2010) and for the poultry industry (Kumari and

Nath, 2018). The challenge may be especially severe for species adapted to relatively narrow temperature ranges (Boyles et al., 2011a; Boyles et al., 2011b), such as birds in the tropic (Huey et al., 2012; Khaliq et al., 2014), and those already operating close to their upper thermal limit such as desert birds (Gerson et al., 2019). However, even birds inhabiting far less extreme, thermally variable, and generally colder habitats, may suffer the negative consequences of acute heat stress (blue tits and great tits; (Andreasson et al., 2018; Rodriguez et al., 2016).

In addition to heat waves, climate change is likely to lead to milder and more unstable winter weather (IPCC, 2014). This aspect has received much less attention than summer heat waves in both physiological and ecological research. Even moderate warming events in winter may cause problems in cold-acclimatized birds: for example Adelie penguins (*Pygoscelis adeliae*) suffered very low reproduction already at temperatures just above 0°C and rainy conditions (Ropert-Coudert, 2014), though it is unclear if this was directly or indirectly linked to thermoregulation. Thus, relative, not only absolute, temperature changes, and the effects of changing temperature on the ecosystem, should always be considered.

Importantly, the most severe challenges may not be posed by temperature per se, but indirectly because mean temperature changes, extremes and changes in humidity are likely to influence food and water availability for birds at all trophic levels (Boyles et al., 2011a; Tieleman and Williams, 1999). We suggest that these indirect changes due to climate change can lead to challenges not only for energy acquisition, but also directly for thermoregulation for birds in hot and dry climates. Specifically, heat loss in birds is only achieved by evaporative cooling when T_b exceeds ambient temperature, and dry heat loss is increasingly less effective as the latter approaches the former. It follows that thermoregulation in hot environments is costly in terms of water (see section §2 and 4). Thus the predicted increases in humidity and/or decreases in water availability ((IPCC, 2014) may further severely influence the capacity of thermoregulation. In line with this, a modelling approach of avian evaporative water requirements and survival times revealed that the IPCC-predicted increases in maximum air temperatures will result in large 150-200% increases in water requirements relative to current values in small birds, which might severely reduce survival during extremely hot weather if water is not available (McKechnie and Wolf, 2010). Indirect effects may also be predicted in cold conditions. For example, it could be speculated that the reduced snow cover and depth that follow increasing winter temperatures might mean that resource availability increases for resident species in the temperate zone. On the other side of the coin, unstable winter weather, especially precipitation as rain and not snow, can lock all available forage as a thick ice crust forms on re-freezing. This has been implicated as the cause of mass mortality events of Arctic grazers (e.g. Forbes et al., 2016), and might well constrict food availability for several bird species in a similar manner.

Finally, climate change does not only concern wildlife but also production animals, as temperatures in rearing facilities cannot always be controlled. Broiler chickens are genetically selected for a fast growth rate, and express high metabolic rate which has impacted their temperature tolerance (Tickle et al., 2018), and makes poultry production susceptible to both high and low environmental temperatures (Tickle and Codd, 2019). To this end, a vast amount of work has been performed to identify the physiological and behavioural responses to heat (and cold) stress to improve production strategies in chicken. These include, for example, selection of suitable breeds, (early-life) nutritional/temperature manipulation, and changes in management and facilities (reviewed in Kumari and Nath, 2018)

6. How to respond to climate change, and the role of endocrine control

Bird species may respond to new thermoregulatory challenges that follow climate change by three mechanisms: 1) populations may shift distributions to track their original environment (range shifts, reviewed e.g in Devictor et al., 2008; La Sorte and Jetz, 2012); 2) individuals within a population may show phenotypic plasticity of thermal and metabolic responses to temperature, either within or across generations; 3) selection may lead to microevolutionary changes (i.e., adaptation) in temperature tolerance or plasticity and its underlying endocrinological and molecular mechanisms. Endocrine mechanisms could play a role in 2 and 3, and are thus discussed here.

6.1. Climate change and plasticity in thermoregulation: scope and speed, costs and constraints

Within-species plasticity of thermoregulation and associated endocrine traits were reviewed in section §4. The potential role of transgenerational plasticity in adapting to climate change has been recently addressed across taxa (Bonduriansky et al., 2012; Cavieres et al., 2019; Donelson et al., 2018; Meylan et al., 2012; Ruuskanen et al., 2016c; Shama et al., 2014; Stillman, 2019). We argue that plasticity via transgenerational/epigenetic adaptation may allow birds to cope better with climate-change related higher/lower *mean temperature*. However, we also speculate that transgenerational or epigenetic 'adaptation' may cause maladaptation and, hence, potentially fitness costs, when increased unpredictability leads to a mismatch. This could occur if temperatures during parental/pre-natal/early postnatal development differ from those that the individual will experience in its future environment, e.g. for birds that develop under the influence of a heat wave. If such changes are not - or only partially - reversible, individuals may be permanently better equipped to deal with thermal conditions they may not again encounter. We argue that for wild birds, this might mostly act on transgenerational effects and post-hatching epigenetic (mal)adaptation, at least in species where parental incubation behaviour is sufficient to buffer pre-natal temperature from dramatic fluctuations (section §4.4). However, it has been recently suggested that embryos may also express considerable physiological and even behavioural plasticity in reptiles and birds (reviewed in Du and Shine, 2015). The capacity for early-life plasticity can be crucial for survival: if extreme events would kill off young before they reach maturity, plasticity in adult individuals will be irrelevant (cf. Burggren, 2018).

Many bird species have excellent capacities to plastically acclimatize to different ambient temperatures during their lifetime (see sections 4.2, 4.3). However, there are constraints and costs of plasticity – otherwise all organisms would be able to adapt to all possible environmental conditions! For example, it has been suggested that the capacity for full acclimatization may occur over a limited temperature range that corresponds to expected temperatures within the geographical range of the species (Norin and Metcalfe, 2019). There is also evidence (from invertebrates) that higher basal temperature tolerance may constrain further acclimatization to temperature (Gerken et al., 2015). Constraints on plasticity in endocrine mechanisms are also likely to exist. For example baseline CORT levels were correlated with the stress-induced CORT response in great tits (Baugh et al., 2014; Hau et al., 2016). Hence, there are likely to be limits to the scope of acclimatization to a changing climate.

With increasing unpredictability, not only the scope, but also *speed of acclimatization* will be crucial to increase survival probability. The latter has rarely been studied. It is conceivable that traits needed to improve thermogenic performance, such as increased tissue and organ size (Swanson and Vezina, 2015) may be slow to respond to acute changes in temperature. Yet, Dubois et al. (2016) reported that the white-throated sparrows (*Zonotrichia albicollis*) show acclimatization of thermogenic performance within just 8 days over 15-20 °C temperature changes. However, over the same time period, black-capped chickadees (*Poecile atricapillus*) and snow buntings (*Plectrophenax nivalis*) did not respond to temperature variation (see also Dubois et al., 2016; Swanson and Olmstead, 1999). Hence, different bird species may vary in the speed, or aptitude, of acclimatization of some traits (see also Swanson and Olmstead, 1999). Moreover, there are indications that the acclimatization to increasing and decreasing temperature is not uniform. Dubois et al. (2016) found that thermogenic capacity was lost at a faster rate when temperature increased, than it was gained when temperature decreased. When considering that thermogenic performance may be linked to overwinter survival (Petit et al., 2017), loss of cold defence mechanisms during increasingly frequent spells of mild winter weather in the temperate region (IPCC 2014) could prove challenging for resident bird species.

Facultative hypo/hyperthermia (§4.2) i.e. short-term, fast and plastic responses, could be utilized to potentially overcome unpredictable, short heat waves or cold snaps. However, many species in cold areas lack capacity for deep hypothermia (McKechnie and Lovegrove, 2002) and so might be more reliant on improved heat-producing capacity than on reduced heat loss rate. Prolonged hyperthermia, on the other hand, will lead to physiological costs, such as oxidative damage to proteins and lipids and can also destabilize the mitochondrial membrane causing an inadvertent increase in proton permeability (reviewed e.g. in Mujahid et al., 2006; Stillman, 2019). This would not only decrease the amount of ATP produced, but also add heat to an already hyperthermic animal, because proton leak is an exothermic process. This certainly limits the capacity of adaptation to frequent/ or long-lasting climate extremes via changes in T_b.

One may speculate that hormonal and associated transcriptomic changes in plastic responses are likely to be relatively fast. In line with this, there is evidence for very rapid cellular responses, such as Na^+K^+ATPase and oxygen consumption to heat treatment in non-model species (house sparrow, *Passer domesticus* Jimenez and Williams, 2014). Behavioral changes are likely to be immediate and may, at least partly, mitigate effects of acute thermal stress. For example, several studies show that the amount of physical work in birds is reduced at high ambient temperature (du Plessis et al., 2012; Powers et al., 2017), presumably to avoid somatic costs of overheating (Nilsson and Nord, 2018). However, such prioritization of self-maintenance may carry fitness costs, as parents risking overheating cannot care optimally for young (Nord and Nilsson, 2019). Moreover, in other cases climate change may render behavioural thermoregulation more difficult. This could be the case for northern birds in winter that might be prevented from snow burrowing, which is integral to their energy balance (e.g. Korhonen, 1981; Marjakangas et al., 1984) as snow cover and depth diminishes and rain-on-snow events become more frequent. This might carry over to endocrine responses to temperature variation: Shipley et al. (2019) found that fecal CORT increases linearly with decreasing environmental temperature in the ruffed grouse (*Bonasa umbellus*), but only when the birds did not use snow burrows.

All in all, while physiological and behavioural plasticity may be sufficient to respond to thermoregulatory needs to average temperature increases, inherent constraints and costs of acclimatization means that responses to weather extremes and an unpredictable climate in the future may not be sufficient in the long-term, and microevolution of thermal physiology may be needed.

6.4. Climate change and microevolution in thermoregulation

A requirement for microevolutionary change in temperature tollerance is that the underlying physiological, endocrinological and molecular mechanisms show genetic variation on which selection can act. Thus we need answers to questions like: Do individuals have different temperature tolerances or differ in their response to temperature changes? Do individuals and populations differ in levels of key hormones and hormonal responses to temperature variation? Do they systematically differ in the scope or speed of acclimatization? Do individuals show different capacities for evaporative cooling?

While individual variation has traditionally been largely ignored in physiological studies (Williams, 2008), there is now increasing interest in such sources of variation (e.g. Taff and Vitousek, 2016). Several key aspects in thermoregulation show individual and potentially genetic variation across taxa: Multiple studies in wild and captive birds report individual variation in BMR, reflected in moderate heritability and repeatability of these traits (Nilsson et al., 2009; Ronning et al., 2007; Tieleman et al., 2009). In one of the rare studies on potential heritability of heat loss mechanisms, Versteeg et al. (2008) reported that evaporative water loss also shows individual variation (repeatability). Moreover, several studies indicated that there is individual consistency in thermoregulatory reaction norms over a temperature gradient. This has been reported in ectotherms such as common lizards (*Zootoca vivipara*, (Artacho et al., 2013) and Western slimy salamanders (*Plethodon albagula* (Careau et al., 2014), and in endotherms such as mouse lemurs (*Microcebus murinus,* (Vuarin et al., 2013) and zebra finches (*Taeniopygia guttata*, Briga and Verhulst (2017). The potential genetic background of such individual plasticity in thermoregulatory reaction norms, has, however, not yet been studied.

Along with variation in metabolism, individual differences in hormonal and molecular responses to temperature variation is predicted, and will be a key in adapting to changing climate. To our knowledge, individual variation in responses to temperature challenges in circulating THs, the key hormones underlying thermoregulation, or associated molecular pathways (DIOs, receptors) has not been tested. However, there is some evidence on heritability of the mean levels of T3 in eggs (Ruuskanen et al., 2016b), suggesting scope for microevolutionary responses of THs to climate change. Interestingly, endocrine responses to thermal stress have been shown to vary among poultry breeds, potentially suggestive of genetic variation in temperature tolerance (Xie et al., 2018). Moreover, there is rather good evidence that individuals consistently differ in their CORT responses to standard stressor

(Cockrem, 2013) as well as e.g. food stress (Lendvai et al., 2014), while CORT shows also moderate heritability (Stedman et al., 2017; Taff et al., 2018). To our knowledge, there is no data on individual plasticity in thermogenesis mechanisms (e.g. NST), mitochondrial function or its molecular basis, such as ANT, avUCP or SERCA expression (see §3) in birds.

Taken together, we still have very limited knowledge on the capacity for microevolution of thermoregulation and its associated endocrine and molecular mechanisms, and we currently lack direct studies on microevolution of thermal physiology in birds. However, some key thermoregulatory and endocrine traits seem to show individual variation with a genetic basis. In mammals, artificial selection for BMR led to changes in 10 generations (Sadowska et al., 2015), which suggests that a response to temperature changes could potentially be rather fast. Interestingly, it has been suggested that current worldwide declining trends of body size of birds (Gardner et al., 2014) could reflect microevolution to climate change as body size critically influences e.g. evaporation. However, even if there would be variation for selection to act on, the most important open question is which traits and mechanisms will/may be under selection in a changing climate. Is there selection on the mean values, or on scope and speed of plasticity when weather changes abruptly? What is the main selective agent? If selective agents like heat waves are rare, selective pressure is low, and microevolution likely plays a little role (Boyles et al., 2011b). However, increasing frequency of extreme events may increase the selective pressure on speed or scope of plasticity, at least if they occur frequently enough to be experienced more than once over the lifetime of an individual.

7. **Conclusions and future directions**

We conclude that while the general patterns in the endocrine regulation of thermogenesis are quite well understood, at least in poultry, the molecular and endocrine mechanisms controlling e.g. mitochondrial function need to be unveiled. In contrast, we have rather poor knowledge on the molecular mechanisms controlling heat loss. Birds express plasticity on a wide range of time scales, from transgenerational and developmental to day-to-day changes in response to environmental temperature variation, but the molecular mechanisms are also poorly described. Importantly, many of those can only be studied in non-model species that live under fluctuating temperature and experience climate change as it is, emphasizing the need for a wide range of study species to understand the scope of plasticity. Plasticity can ameliorate climate change effects on thermoregulation to some extent. However, the increased frequency of extreme weather events may be beyond the scope or speed for plastic responses, and so may potentially result in mass mortality (Gardner et al., 2017; McKechnie and Wolf, 2010) and selection for more tolerant phenotypes. To understand which traits can respond to selection, more studies on genetic variation in thermoregulation, its plasticity, and underlying endocrine and molecular mechanisms are needed. The combination of climate change related effects, that include alterations in humidity, precipitation patterns and primary production, are likely to pose even greater challenges for plastic thermoregulatory phenotypes. The underlying endocrine and molecular mechanisms involved in such responses to the changing world, and their costs and constraints, should be studied more closely. We must also remember that even minor changes in absolute temperature can bring cascading effects to the ecosystems in which birds live, with potential negative feedback on several aspects of thermoregulation. Below, we outline some future directions:

(i) *Individual and population-level variation in endocrine responses to temperature*

To understand how populations and species may respond to changing temperatures, plasticity, its costs and constraints, and potential for microevolution, we need more studies on the individual reaction norms on endocrine and metabolic traits, and underlying molecular mechanisms, as well as on the correlation between baseline and speed and slope of change.

(ii) *Transgenerational/epigenetic adaptation and endocrine mechanisms* To understand transgenerational effects and developmental programming of thermoregulation, the molecular and endocrine mechanisms of transgenerational and epigenetic adaptation should be further addressed, especially in the context of persistence of such effects to adulthood.

(iii) *Beyond model species* Given the enormous variation in temperature tolerances across species (and populations), and even completely different regulatory mechanisms (e.g. heat dissipation, occurrence of facultative hypo/hyperthermia, behaviour) between species, studies need to be extended beyond domesticated models to mirror the interspecific variation in endocrine or other physiological responses to changing climate.

(iv) *From the lab to the field* Results of laboratory studies on acclimation are difficult to use in predicting how thermal physiology will be affected in wild populations where climate-change effects on temperature, humidity, and food availability can act synergistically on selection for thermal phenotypes. Similarly, behavioural strategies and movement that influence temperature tolerance in the field populations can only be simulated in the lab with difficulty.

(v) *More realistic experimental designs* Following from the previous points, experimental designs testing thermal physiology should include multiple interacting factors as well as temporal stochasticity to yield more realistic estimates of how thermoregulatory and endocrine traits may be affected by climate change.

(vi) *Influences of temperature beyond thermal physiology* This review has focused on the associations between changing temperature and thermoregulation. However, for many seasonally breeding birds, temperature also functions as an important cue (supplementary to photoperiodic cues) to adjust the timing of breeding, and other life-history events (Caro et al., 2013). Thus, to understand the complex influences of temperature on organismal physiology and phenotype, the multiple effector roles of temperature need to be considered.

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Figure legends

Fig 1. A simplified schematic figure of the mechanisms of thermoregulation in birds and putative key endocrine and neuronal mechanisms underlying each response (modified from Yahav, 2015). PO/AH = preoptic anterior hypothalamus, THs = thyroid hormones, CORT= corticosterone, AVT= arginine vasotocin, CNS = central nervous system, SNS= sympathetic nervous system, TNZ = thermoneutral zone.

Fig 2. A schematic diagram of the potential pathways of THs on thermogenesis below thermoneutral zone. UCP = uncoupling protein, ANT = adenine nucleotide translocase, SERCA = Ca2+ ATPase. See text for references.

Fig 3. Schematic diagram of plasticity in thermoregulation at different time-scales, and associated putative molecular and endocrine mechanisms. See text for references.

Fig. 4. Key thermoregulatory challenges in birds in changing climate.

Fig 1.

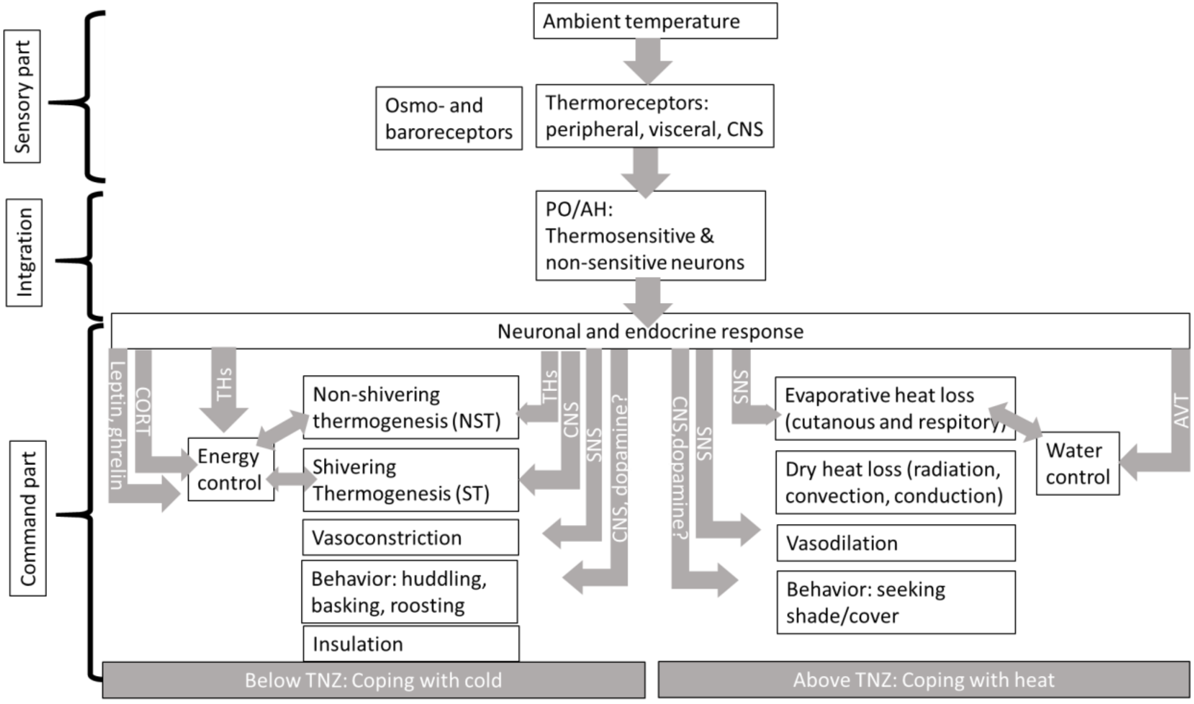

Sensory part
Intgration
Command part
Ambient temperature
Osmo- and baroreceptors
Thermoreceptors: peripheral, visceral, CNS
PO/AH: Thermosensitive & non-sensitive neurons
Neuronal and endocrine response
Leptin, ghrelin
CORT
THs
Energy control
Non-shivering thermogenesis (NST)
Shivering Thermogenesis (ST)
Vasoconstriction
Behavior: huddling, basking, roosting
Insulation
THs
CNS
SNS
CNS, dopamine?
CNS,dopamine?
SNS
SNS
Evaporative heat loss (cutanous and respitory)
Dry heat loss (radiation, convection, conduction)
Vasodilation
Behavior: seeking shade/cover
Water control
AVT
Below TNZ: Coping with cold
Above TNZ: Coping with heat

Fig 2.

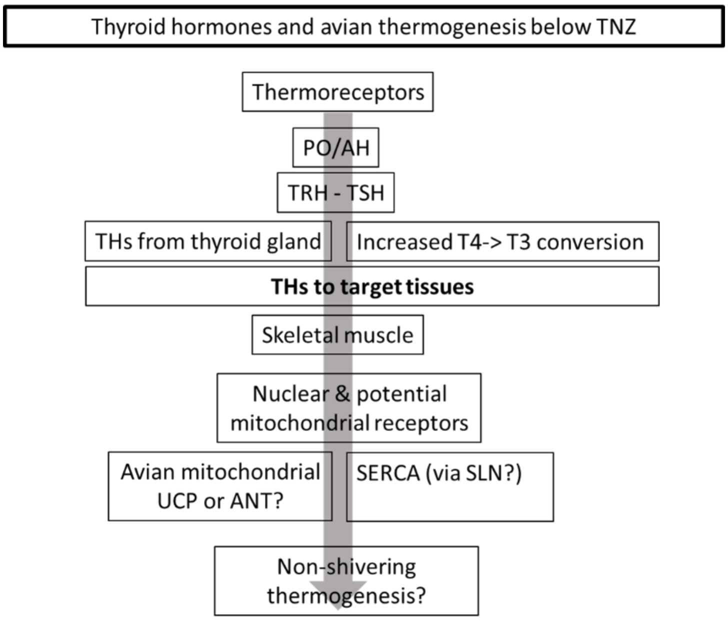

Thyroid hormones and avian thermogenesis below TNZ
Thermoreceptors
PO/AH
TRH - TSH
THs from thyroid gland
Increased T4-> T3 conversion
THs to target tissues
Skeletal muscle
Nuclear & potential mitochondrial receptors
Avian mitochondrial UCP or ANT?
SERCA (via SLN?)
Non-shivering thermogenesis?

Fig 3.

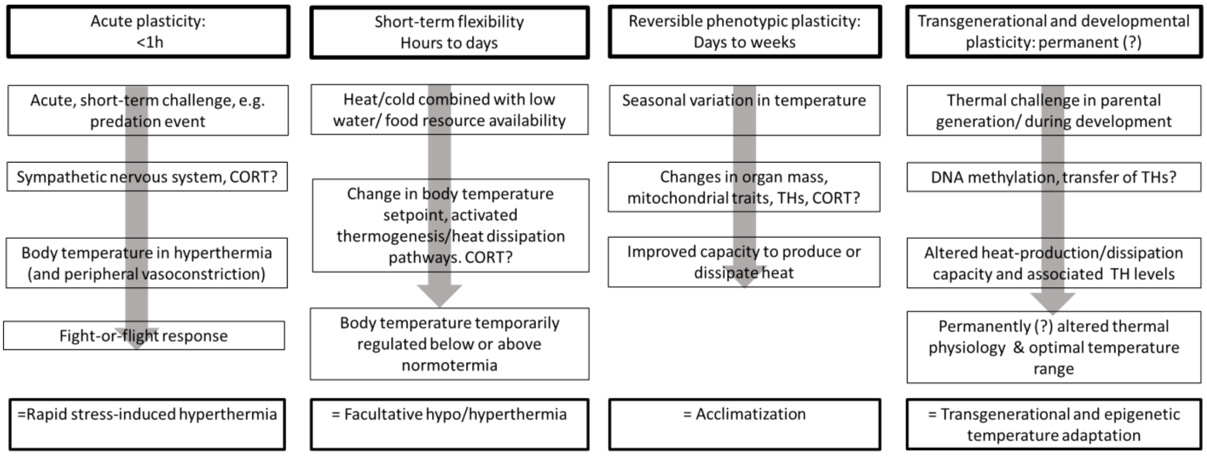
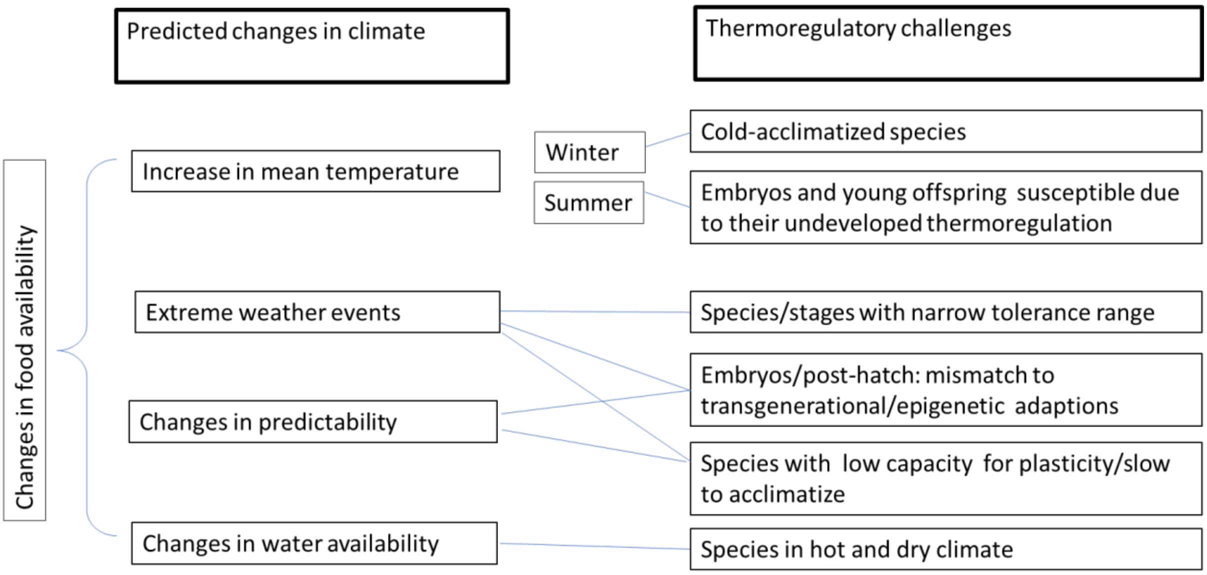

Acute plasticity: <1h
Acute, short-term challenge, e.g. predation event
Sympathetic nervous system, CORT?
Body temperature in hyperthermia (and peripheral vasoconstriction)
Fight-or-flight response
=Rapid stress-induced hyperthermia
Short-term flexibility Hours to days
Heat/cold combined with low water/ food resource availability
Change in body temperature setpoint, activated thermogenesis/heat dissipation pathways. CORT?
Body temperature temporarily regulated below or above normotermia
= Facultative hypo/hyperthermia
Reversible phenotypic plasticity: Days to weeks
Seasonal variation in temperature
Changes in organ mass, mitochondrial traits, THs, CORT?
Improved capacity to produce or dissipate heat
= Acclimatization
Transgenerational and developmental plasticity: permanent (?)
Thermal challenge in parental generation/ during development
DNA methylation, transfer of THs?
Altered heat-production/dissipation capacity and associated TH levels
Permanently (?) altered thermal physiology & optimal temperature range
= Transgenerational and epigenetic temperature adaptation

Fig. 4.


Predicted changes in climate
Thermoregulatory challenges
Changes in food availability
Increase in mean temperature
Winter
Summer
Cold-acclimatized species
Embryos and young offspring susceptible due to their undeveloped thermoregulation
Extreme weather events
Species/stages with narrow tolerance range
Embryos/post-hatch: mismatch to transgenerational/epigenetic adaptions
Changes in predictability
Species with low capacity for plasticity/slow to acclimatize
Changes in water availability
Species in hot and dry climate