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Physiological mechanisms mediating the trade-off between survival and reproduction in birds

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Abstract

Despite an abundance of evidence in support of a trade-off between survival and reproduction in birds, we still have a limited understanding of the physiological mechanisms allowing this trade-off to persist. In this review, I discuss three physiological pathways hypothesized to mediate the trade-off between survival and reproduction in birds: 1) baseline corticosterone, 2) oxidative stress, and 3) immune function. While I found evidence in the literature in support of each of these pathways as a mechanism mediating this trade-off, there are still many questions that remain unanswered for each of the proposed mechanisms. In particular, given that these mechanisms are unlikely to be mutually exclusive, there is currently a lack of research incorporating interactions between mechanisms. I suggest that future research should include multiple mechanisms and their interactions as a sufficient effect size of the trade-off between survival and reproduction may only be detected when these are considered.

Keywords — life history, costs of reproduction, corticosterone, oxidative stress, immune function, reproductive investment

1. Introduction

The trade-off between survival and reproduction is one of the central tenants of life history theory and is documented in many taxa including fish, insects, mammals, reptiles, and birds [1, 2]. The resource allocation hypothesis postulates that in an environment with finite resources an investment of resources in reproduction has the capacity of reducing survival because these resources can no longer be directed towards self-maintenance [2]. In birds, there is strong, but some contradictory (see [3]), evidence for this trade-off with the costs of reproduction arising from several breeding stages not limited to chick-rearing and incubation [3]. Despite the impressive amount of evidence in support of this trade-off, far less is known of the physiological mechanisms responsible [1, 4]. In this review I first discuss three of the proposed physiological pathways mediating the trade-off between survival and reproduction in birds: 1) baseline corticosterone, 2) oxidative stress, and 3) immune function. After, I discuss the need for future research to focus both on pathways of individual mechanisms and potential interactions between mechanisms.

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2. Baseline corticosterone

The hormone corticosterone (CORT) may be able to mediate the costs of reproduction through its role in mobilizing energy stores [5]. Controlled by the hypothalamic-pituitary-adrenal (HPA) axis, CORT serves the primary function of maintaining adequate glucose and free fatty acid levels in the blood through stimulation of gluconeogenesis and lipolysis. The baseline levels of CORT maintained in the blood stream are pivotal to survival as baseline CORT levels have downstream effects on the levels of e.g. glucose, free fatty acids, hematocrit, reproductive hormones, immunosuppression, oxidative stress, and telomere length, many of which have been linked to survival in vertebrates [6, 7, 8, 9]. CORT values rise during extended periods of increased activity or stress to mobilize energy stores, potentially during reproduction, and thus baseline CORT may serve as a mechanism of mediating the costs of reproduction [5].

Evidence in support of CORT as a mediator of the trade-off between survival and reproduction through mobilization of energy stores for current resource demand is equivocal. The Cort-Fitness Hypothesis proposes that CORT levels should increase with declines in reproductive success because CORT is involved in response to environmental challenges and increased environmental challenges cause reallocation of resources from reproduction to respond to these challenges [10]. However, studies testing the Cort-Fitness Hypothesis present contradictory results with no relationship between CORT and reproductive success [11], a positive correlation [12], and the predicted negative correlation [11, 13]. For example, non-manipulated European starlings (*Sturnus vulgaris*) raising offspring had higher baseline CORT levels compared to those not raising offspring [14]. In contrast, chronically stressed barn swallows (*Hirundo rustica*) had increased glucocorticoid levels associated with declines in reproductive success through the production of lower quality offspring [15]. One potential explanation for these conflicting results is the use of inconsistent or inadequate metrics to measure baseline CORT.

While most studies measure the total level of CORT in circulation as a metric of baseline CORT, this may be an insufficient metric because hormone effects are modified by binding proteins in the blood [16]. Specifically, CORT binds to corticosteroid-binding globulin (CBG), which functions to transport CORT to various tissues via the circulatory system. There is now substantial evidence demonstrating that the biologically active fraction of CORT consists only of the portion that is free i.e. not bound to CBG. This suggests that the measurement of free CORT is more biologically relevant than the measurement of total CORT, despite its less frequent use in the literature [9]. The discrepancy across studies in measuring total CORT vs. free CORT levels may be able to explain some of the contradictory results discussed above. Additionally, the effects of CORT depend on cell-specific receptor mechanisms such as mineralocorticoid receptors (MR) and glucocorticoid receptors (GR). If the effects of CORT are mediated by the availability of these receptors, then a measurement of their availability would also be meaningful to include when assessing the impact of CORT [17]. Finally, measurements of upstream mediators of CORT production such as Corticotrophin Releasing Hormone (CRH) and Adrenocorticotropic Hormone (ACTH) may also be relevant if either are the limiting factor in determining circulating levels of CORT [18]. Considering a wider range of metrics involved in the CORT stress response may allow us to deepen our

understanding of the mechanisms by which CORT mediates the trade-off between survival and reproduction.

The inability of the Cort-Fitness Hypothesis to reliably make predictions may also suggest that CORT plays a more complex role in responding to current resource demand in mediating the trade-off between survival and reproduction. In response to an inconsistent relationship between CORT and reproductive success across breeding stages in tree swallows (*Tachycineta bicolor*), where females with heavier clutch masses had lower CORT levels early in breeding whereas females raising broods with the greatest mass had elevated CORT levels, Bonier et al. [19] proposed that the Cort-Fitness Hypothesis be modified to the Cort-Adaptation Hypothesis. According to this hypothesis, when an individual makes a decision to reproduce, a negative relationship between baseline CORT and reproductive investment is expected because individuals facing less environmental stress can invest more in reproduction. After an individual invests heavily in reproduction CORT levels should positively correlate with reproductive success because this increased investment in reproduction requires increased CORT levels to allocate energy to reproduction [19]. This hypothesis is able to explain the variation in the relationship between reproductive investment and CORT across time within individuals and the results are reproducible across several other species [20, 21, 22]. For example, European starlings (*Sturnus vulgaris*) increased baseline CORT levels in preparation of reproductive investment and thus used CORT as a mechanism to manage investment decisions across reproductive attempts to maximize fitness [21]. Love et al. [15] concluded that CORT is able to mediate the trade-off between reproduction and survival in birds through management of reproductive investment annually to optimize lifetime reproductive success. This suggests that CORT mediates this trade-off through management of long-term reproductive investment in addition to current resource demand, and future research should be directed towards understanding mechanistically how CORT mediates future vs. current resource demand. Additional work may also focus on linking changes in CORT levels to changes in survival (although some studies have already done this, see [23]). Given that CORT is believed to influence survival indirectly via its downstream effectors (e.g. glucose, free fatty acids, oxidative stress, immunosuppression, telomere length etc.), it may be beneficial for future studies to include measurements of these downstream effectors in addition to measurements of total and free CORT [9].

3. Oxidative stress

Oxidative stress has the capacity to mediate the trade-off between survival and reproduction in birds through its production as a result of metabolic demand and association with aging [24]. Aerobic species, including birds, use oxygen for efficient energy release during metabolic processes, resulting in the production of reactive oxygen species [19, 20, ROS]. These ROS function as signaling molecules [25], but are also highly unstable and cause damage to membranes, proteins, lipids, and DNA. Oxidative stress occurs when antioxidant molecules are unable to fully neutralize ROS resulting in damage to biomolecules [26, 27]. This mechanism may be used to mediate the costs of reproduction as an increase in energy demand during reproduction results in an

increase in production of ROS and, if not enough antioxidants are produced, an increase in biomolecule damage occurs, contributing to aging and hence survival [24, 28].

Quantifications of the trade-off between reproduction and survival using antioxidant measures have produced indefinite results [24]. Many studies observe the predicted negative relationship between reproductive effort and antioxidants or the overall antioxidant capacity of the blood [29, 30, 31, 32, 33]. For example, male zebra finches (*Taeniopygia guttata*) with experimentally enlarged brood sizes experienced decreases in antioxidant enzyme activity [33]. However, the relationship between antioxidants and survival remains less clear with some evidence for a positive relationship between antioxidant capacity and survival [34, 35] and other evidence for no association between antioxidant status and survival [36, 37]. Theoretically, antioxidant status should correlate positively with survival if higher levels of antioxidants result in less oxidative stress and delayed senescence. It is important to note however, that measures of antioxidants do not provide a direct measure of oxidative stress as an increased level of antioxidants may be coupled with an increase in ROS, resulting in no change in oxidative damage. Thus to get a more accurate measure of oxidative stress an additional measure of the amount of ROS is necessary [24]. Several studies provide support for an oxidative cost of reproduction when oxidative stress is measured as the ratio of reactive oxygen metabolites to antioxidants, however few studies have used this approach [37, 38] and there are also results from it suggesting no oxidative cost of reproduction [39]. This inconsistency in results suggests that antioxidants may have a more complex relationship with the costs of reproduction or are an inadequate measure of oxidative stress.

Another approach to measuring oxidative stress, via direct measurement of oxidative damage to biomolecules, supports oxidative stress as a mediator of the trade-off between survival and reproduction. For example, a non-manipulative study of Florida scrub jays (*Aphelocoma coerulescens*) found an increase in oxidative damage to proteins in males post-breeding [40]. This suggests that reproduction increased oxidative stress, likely through an inability of antioxidants to match increases in ROS. Further support for this exists as increased oxidative damage, resulting from increased reproductive effort, is associated with no change in antioxidant status [41] and increased levels of antioxidants during reproduction are associated with no change in oxidative damage [36]. Interestingly, a recent meta-analysis by Blount et al. [42] revealed that while oxidative damage is frequently positively associated with reproductive effort in females, breeding females paradoxically have lower oxidative damage compared to non-breeding females. This suggests that the costs of reproduction may be mediated by 1) increases in oxidative damage associated with reproductive effort and 2) the cost of mechanisms utilised by females to minimise such damage i.e. oxidative shielding [42]. Further work is needed to understand how significant the cost of diminishing oxidative damage is for females and if it, alone and combined with the effects of oxidative damage, can have a significant impact on survival.

The inconsistent use of metrics to measure oxidative stress is a significant limiting factor in this field. The number of studies that address direct oxidative damage is limited and of the ones that do, there is not a wide enough range of tissues being measured as damage may be tissue-specific [43]. Thus while there is evidence in support

of oxidative stress as a mediator of the trade-off between survival and reproduction, this support should be interpreted with great caution [43]. That results depend on the measure of oxidative stress used suggests that we have little scope for how this mechanism mediates the costs of reproduction and that future research is needed measuring a wider range of tissues and including measurements of ROS, antioxidants, oxidative damage, and repair mechanisms to improve our understanding [44].

4. Immune function

Immune function is hypothesized to mediate the trade-off between survival and reproduction in birds through an energetic trade-off [45, 46, 47]. Reproduction and immune defenses are both energetically costly such that an increase in reproductive effort should lead to a decrease in immune function resulting in increased susceptibility to parasitism and thus reduced survival [48, 49]. Two predictions resulting from this model are that a positive relationship should be observed between reproductive effort and levels of parasitism and a negative relationship between reproductive effort and immune response [50]. Evidence supporting these predictions is mixed with some studies supporting both of the predicted relationships [51, 52], some providing no support for an effect of reproduction on parasitism [53], and others providing no support for an effect of reproduction on immune function [54]. However, a meta-analysis on this topic by Knowles et al. [50] found an overall weak, but well supported positive effect of reproductive effort on blood parasite levels and a moderate negative effect of reproductive effort on immune responsiveness. Additionally, inconsistencies in results were largely dependent upon experimental design and the length of time between manipulation of reproductive effort and measurement, with results suggesting that immunosuppression increases with the length of the chick-rearing period. For example, Skylarks (*Alauda arvensis*) handicapped with additional weight experienced no change in immune function during their first brood, however immune function during their second brood was able to predict return rates the following year [55]. Inconsistent results may also be explained by variation in metrics used to measure parasitism and immune responsiveness.

Similar to the CORT stress response and oxidative stress, there are a variety of metrics that have been used to document immune function in birds. Moreover, a single metric is unlikely to capture the complexity of immune function [56]. Parasitism can be measured with 1) prevalence (the proportion of the population that is infected) or 2) parasitaemia (the number of parasites in an infected host). Weaker effect sizes have typically been seen in studies using prevalence as a measure of parasitism [50]. This may be because studies were not long enough to capture changes in prevalence due to long periods of prepatency in hosts (i.e. the parasite is present, but not at high enough levels to be detected). Further, prevalence may be more dependent on environmental factors that influence host exposure and transmission. Alternatively, immune function can also be measured as the immune response to a novel antigenic challenge (e.g. sheep red blood cells). But there is no consistent novel antigenic challenge used across studies and it is unclear how an immune response to a novel antigen relates to host-parasite interactions in the host' natural environment [50]. Further, depending on the metric

used to measure immune response (e.g. leukocyte proportions), different measurements may have bias towards innate or adaptive immunity. While innate immunity requires investment early in life, adaptive immunity is developed later in life upon encountering novel pathogens and is therefore more likely to play a larger role in explaining the trade-off between reproduction and survival. It is possible that studies using metrics that better capture adaptive immunity will be more likely to detect an energetic trade-off between survival and reproduction.

There is currently no consensus of the currency that may allow immune function to mediate the trade-off between survival and reproduction. Evidence in support of an energetic cost is weak as the 5-15% increases in metabolic rate associated with an immune response are insignificant compared to the 300-400% increases during breeding [57]. While this may be important for a highly resource-limited individual, other explanations should be considered such as an adaptive suppression of the immune system during breeding to protect against harmful autoimmune responses [58] or increased damage to immune cells due to oxidative stress [57]. However, evidence supporting these mechanisms is also limited and often contradictory [57]. For example, male great tits (*Parus major*) rearing enlarged broods had increased parasite levels and decreased resistance to oxidative stress but no relationship between the two, suggesting independent mechanisms [59]. Overall this suggests we know very little of how immune function can limit the trade-off between survival and reproduction.

Regardless of the mechanism linking reproductive effort and immune function, one remaining question is whether changes in immune function can contribute significantly to changes in survival. While there is general support in the literature for a link between immune response and survival [60] the relationship between parasite infection and survival is less clear [50]. This may be because wild birds caught are more likely to be in the chronic infection phase which is rarely associated with survival effects [61, 62] or because the increases in parasite levels are insufficient alone to account for reduced survival because the costs of reproduction are felt along multiple pathways [59]. Thus while there is support for immune function as a mediator of the trade-off between reproduction and survival, further research is necessary both to understand the mechanism mediating the trade-off between reproduction and immune function as well as how immune function alters survival.

5. Conclusion

Despite the strong evidence in support of a trade-off between survival and reproduction in birds, we still know very little of how the proposed mechanisms are able to mediate this trade-off [1, 4]. While baseline CORT, oxidative stress, and immune function are supported mediators of this trade-off, our understanding of their mechanisms is limited. One obstacle impeding our progress in understanding the mechanisms behind all three physiological pathways is the inconsistent use of metrics. Advances in this field will likely be limited until adequate metrics are implemented universally. It is also clear that each of the proposed pathways does not act independently from the rest. For example, the effects of CORT on survival are mediated through immunosuppression [63, 64] and oxidative stress [64]. Similarly, immune response may be reduced during

reproduction due to increased damage to immune cells from oxidative stress [57]. Future research should not be limited by studying each of the mechanisms as mutually exclusive pathways. Instead, there is a need to focus both on pathways of individual mechanisms and potential interactions between mechanisms, as sufficient effect sizes may only be detected when multiple mechanisms and their interactions are considered. While some researchers have attempted to study multiple mechanisms together, e.g. male great tits (*Parus major*) rearing experimentally enlarged broods had increased parasite levels *and* decreased resistance to oxidative stress [59], the number of studies utilizing this kind of approach is limited. Where this approach may be particularly valuable is in studying the effect of potential physiological mediators of this trade-off on survival. For example, experimentally increasing levels of parasitism may not allow for detection of a significant effect on survival if multiple pathways interact with immune function to produce a significant survival effect. Instead, levels of parasitism could be manipulated in conjunction with levels of glucocorticoids and oxidative stress and the effect on survival measured. While there are drawbacks to this approach e.g. increased experimental design complexity, the current state of knowledge in this field requires the advancement to potentially more complex experimental designs to further our understanding of the mechanisms mediating this pivotal trade-off.

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