



Cold temperatures induce priming of the glucose stress response in tree swallows

Thomas A. Ryan^{a,b,*}, Conor C. Taff^{a,b}, Cedric Zimmer^c, Maren N. Vitousek^{a,b}

^a Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, NY, USA

^b Cornell Lab of Ornithology, Ithaca, NY, USA

^c Laboratory of Experimental and Comparative Ethology, University Sorbonne Paris Nord, Villetaneuse, France

ARTICLE INFO

Editor: Michael Hedrick

Keywords:

Glucose regulation
Acute stress
Weather
Phenotypic plasticity
Birds

ABSTRACT

Capricious environments often present wild animals with challenges that coincide or occur in sequence. Conceptual models of the stress response predict that one threat may prime or dampen the response to another. Although evidence has supported this for glucocorticoid responses, much less is known about the effects of previous challenges on energy mobilization. Food limitation may have a particularly important effect, by altering the ability to mobilize energy when faced with a subsequent challenge. We tested the prediction that challenging weather conditions, which reduce food availability, alter the energetic response to a subsequent acute challenge (capture and restraint). Using a three-year dataset from female tree swallows measured during three substages of breeding, we used a model comparison approach to test if weather (temperature, wind speed, and precipitation) over 3- or 72-hour timescales predicted baseline and post-restraint glucose levels, and if so which environmental factors were the strongest predictors. Contrary to our predictions, weather conditions did not affect baseline glucose; however, birds that had experienced lower temperatures over the preceding 72 h tended to have higher stress-induced glucose when faced with an acute stressor. We also saw some support for an effect of rainfall on stress-induced glucose: around the time that eggs hatched, birds that had experienced more rainfall over the preceding 72 h mounted lower responses. Overall, we find support in a wild animal for the idea that the glucose stress response may be primed by exposure to prior challenges.

1. Introduction

Wild animals live in variable environments, which have the potential to quickly change in life-threatening ways. Fine-tuned stress response systems have evolved to help animals handle these mercurial environments (Wingfield et al., 1998; Wingfield, 2005). The ability to mobilize the requisite energy in response to challenging environmental conditions is a crucial aspect of stress response systems (Dallman et al., 1993). The metabolic component of the vertebrate stress response is characterized by the rapid mobilization of glucose through the combination of catecholamine-mediated inhibition of glucose uptake by peripheral tissues and stimulatory effects on hepatic gluconeogenesis and glycogenolysis (Munck, 1971; Davies and Lefkowitz, 1984; Remage-Healey and Romero, 2000; Dallman and Bhatnagar, 2011; Romero and Beattie, 2022). Glucose elevation helps to produce energy, both through cellular oxidation and by mediating various metabolic processes, including glycogen and fatty acid synthesis (Braun and Sweazea, 2008; Weber,

2011). Glucose may be secondary to lipids or proteins as an energy source for some taxa (particularly birds) and during certain metabolic challenges, such as migration (Gerson and Guglielmo, 2011; Kuzmiak et al., 2012). Glucose also plays a role in energy balance under normal (non-acute stress) conditions. Maintaining sufficient glucose levels under standard conditions is important, as critically hypoglycemic individuals may lack sufficient energy to survive (Akiba et al., 1999). However, high glucose levels may also be costly. Prolonged hyperglycemia can cause oxidative stress resulting in serious tissue damage and advanced cellular aging, although birds may be better equipped to handle oxidative stress than mammals due to comparatively higher antioxidant levels (Scanes and Braun, 2013; Récapet et al., 2016; Montoya et al., 2018; but see, Ku and Sohal, 1993, Braun and Sweazea, 2008, Smith et al., 2011).

Evidence from a variety of sources suggests that glucose rises in response to acute stressors (Carragher and Rees, 1994; Sapolsky et al., 2000). This effect on glucose—and its mediation by glucocorticoids

* Corresponding author at: 215 Tower Rd., Ithaca, NY 14853, USA.

E-mail address: tar87@cornell.edu (T.A. Ryan).

<https://doi.org/10.1016/j.cbpa.2023.111419>

Received 8 December 2022; Received in revised form 6 March 2023; Accepted 21 March 2023

Available online 23 March 2023

1095-6433/© 2023 Published by Elsevier Inc.

specifically—may be greater in fasted animals, but seems to be a general response that is thought to help organisms recover energetically following acute stress and prepare for future challenges (McGuinness et al., 1993; Jessop et al., 2003; Romero and Beattie, 2022; but see Thurston et al., 1993; Remage-Healey and Romero, 2000; Remage-Healey and Romero, 2000). This general pattern is not present in all species (Fokidis et al., 2011) or consistent across life history stages (Deviche et al., 2016), but has been illustrated in wild tree swallows (*Tachycineta bicolor*; Taff et al., 2022), which show consistent glucose elevation following an acute stressor, and a further increase following injection with adrenocorticotropin releasing hormone (ACTH), a tropic hormone that stimulates the secretion of glucocorticoids. However, variation in the corticosterone response does not predict variation in the glucose response to stress in wild swallows, rufous-winged sparrows (*Peucaea carpalis*), or wandering gartersnakes (*Thamnophis elegans vagrans*), illustrating an incomplete understanding of what modifies the glucose response to stress (Deviche et al., 2016; Neuman-Lee et al., 2019; Taff et al., 2022).

Across birds, species with lower body mass have stronger glucose responses, a pattern that may reflect a greater need to mobilize energy quickly in smaller species (Tomasek et al., 2019). Some species show a similar pattern within populations; for example, tree swallows with lower body mass have higher baseline glucose (Taff et al., 2022). However, in a comparative study of two species of sparrows that elevated glucose in response to acute stress body fat score predicted stress-induced glucose levels in one species, but not the other (Malisch et al., 2018). Given the apparent relationships between energetic demand and baseline glucocorticoids, it may be adaptive for glucose regulation to be responsive to environmental fluctuations that affect risk or energetic demand; however, little is known about how glucose regulation varies by environment. Temperature and baseline glucose have been shown to covary negatively in some species (Schradin et al., 2015), but positively in others (Gangloff et al., 2016), and in opposite directions—depending on heat or cold exposure and timescale—in captive pigeons, *Columba livia* (Jeronen et al., 1976). Baseline glucose also increases during the rainy season in tropical birds, indicating a possible positive association of precipitation and baseline glucose (Tomásek et al., 2022). Prior work also shows that the glucose response to acute stress can vary across life history stage (Deviche et al., 2016) and habitat (a proxy for predation environment: Hik et al., 2001), however, the nature of these relationships is not always consistent across species (Boonstra et al., 1998; Taff et al., 2022).

Another major unknown question is how glucose regulation is affected by multiple challenges. Much of the research on glucose stress responses has focused on the effect of a single discrete stressor. However, the challenges posed by natural environments are complex and often include sets of multiple sequential or coinciding stressors (Romero, 2004; Boussaid-Om Ezzine et al., 2010; Taff and Vitousek, 2016; Malkoc et al., 2022). Conceptual models and empirical studies of other components of the stress response, particularly glucocorticoids, indicate that one challenge has the potential to alter responses to subsequent challenges (Sapolsky et al., 2000; Romero et al., 2009; Sadoul et al., 2015; Del Giudice et al., 2018). Depending on the context a dampened or a heightened stress response to a subsequent stressor could have a positive or negative effect on organismal fitness. For example, a dampened stress response could impede the ability of organisms to respond effectively to future stressors (Busch et al., 2008), or help to protect an organism from the negative effects of high glucocorticoid levels (Wingfield and Sapolsky, 2003). Alternatively, “preparative” or “priming” effects that increase the physiological response to future challenges could enable organisms to better meet or recover from those challenges (Sapolsky et al., 2000; Hilker et al., 2016), or increase the likelihood of deleterious effects from exposure to high glucocorticoid levels (Del Giudice et al., 2018).

Here, we ask if weather conditions influence the regulation of blood glucose levels in breeding, adult tree swallows (*Tachycineta bicolor*).

Tree swallows are among the earliest songbird migrants to return from wintering grounds to breed in North America, and are often faced with periods of cold weather during the beginning of the breeding period. As aerial insectivores, their food availability is highly dependent on daily maximum temperature (Winkler et al., 2013), and may also be influenced by windspeed and precipitation (Irons et al., 2017; Cox et al., 2019; but see Imlay et al., 2017). At our primary study site in Ithaca, NY, most aerial insects only emerge when daily maximum temperatures exceed ~18.5 °C (Winkler et al., 2013). Severe cold snaps, which also increase the thermoregulatory costs of adults and nestlings, result in declines in body mass and widespread reproductive failure (Winkler et al., 2013; Ouyang et al., 2015; Shipley et al., 2020; Garrett et al., 2022). Although less is known about the impact of rain and wind on insect availability or tree swallow condition, these variables can also impact overall reproductive success (Cox et al., 2019; Garrett et al., 2022) and the timing of breeding (Irons et al., 2017).

We tested the hypothesis that environmental variables would affect baseline and stress-induced glucose levels in breeding female tree swallows. Following difficult weather conditions for breeding tree swallows—lower temperatures, higher precipitation, and higher wind speed—we predicted an increase in baseline glucose due to increased energetic demand to recover from the preceding harsher conditions. An alternative possibility, however, is that poor weather conditions might impair energy intake, and lead to a baseline glucose decrease during inclement weather. We also tested whether environmental conditions affect the acute glucose stress response. We predicted that experiencing an energetic challenge would impair the ability to respond to future challenges, and thus, that birds that experienced suboptimal environmental conditions (temperatures and/or higher rainfall and/or wind-speed) would exhibit dampened stress-induced glucose levels in response to a subsequent stressor. Alternatively, if experiencing an energetic challenge primes the glucose response to future challenges, then following suboptimal weather conditions birds might exhibit heightened stress-induced glucose in response to a subsequent stressor. We also predicted that temperature would have a stronger effect on glucose levels than windspeed or precipitation. We further predicted that longer-term weather patterns (previous 72-h) would have a greater impact on glucose than current conditions (previous 3-h). Finally, we predicted that both baseline and stress-induced glucose levels would be higher at later breeding substages, reflecting an increased difficulty in responding to and recovering from sequential challenges while provisioning nestlings.

2. Methods

We studied a population of tree swallows that breed in nest boxes at three adjacent sites in Tompkins County, near Ithaca, NY (42.505°N, -76.466°W; 42.503°N, -76.437°W; 42.460°N, -76.368°W) from 2016 to 2018. Once breeding activity begins, tree swallow nest boxes are checked every other day, and daily during the expected hatching period, to allow for accurate monitoring of breeding stage and nest activity. Females were captured up to 3 times throughout the breeding season. Captures were made by hand at the swallow’s nest box, or occasionally with the aid of an internally placed and manually-triggered trap. The first capture (“incubation” samples) took place on day 6–7 of incubation in all years. The second capture (“near-hatching” samples) took place on either day 12–13 of incubation (2016) or day 1–2 of nestling provisioning (2017–2018). The third capture (“provisioning” samples) occurred on day 6–7 of nestling provisioning in all years. Blood samples from females captured less than three times during the season, which primarily resulted from nest failure, were included in the analysis. All captures occurred between 0700 and 1000 h to reduce the impact of circadian patterns in circulating glucose. This specific sampling window, which is used consistently in our long-term study, was selected because female tree swallows are easiest to capture at this time of day.

At each capture, blood samples were taken via brachial venipuncture

with a 27-gauge needle and collected in capillary tubes. An initial blood sample of $\sim 70\mu\text{L}$ was taken within 3 min of capture to measure baseline circulating glucose levels in the blood and a second blood sample of $\sim 35\mu\text{L}$ was taken after 30 min of restraint in a cloth bag to measure stress-induced circulating glucose levels (Wingfield and Romero, 2011). Immediately after each blood sample was collected, glucose was measured directly from whole blood using a FreeStyle Lite Glucose Meter and test strips (Abbott Laboratories; Breuner et al., 2013). Prior work on glucose in this population of tree swallows has validated the use of this meter for measuring glucose in this manner (Taff et al., 2021). Between the baseline and stress-induced samples, swallows were weighed with a Pesola scale to the nearest 0.25 g and other morphological measures (length of combined bill and head, wing length) were taken.

Hourly weather data from the Game Farm Road Weather Station (Ithaca, NY), approximately 7 km away from all three field sites (42.445° N, -76.448° W), were downloaded from the Northeast Regional Climate Center website (www.nrcc.cornell.edu/wxstation/ithaca/ithaca.html) for use in weather analysis. For each capture event where glucose was measured, we calculated average temperature, wind speed, and precipitation on the morning of capture (3 h before capture) and for three days prior to capture (72 h). Ambient temperature over the latter interval best predicts the regulation of stress-induced corticosterone in tree swallows (Vitousek et al., 2022); 3-day cold snaps have also been found to be most predictive of the likelihood of nest abandonment in this population (Winkler et al., 2013).

Weather-based predictors of baseline and stress-induced glucose levels were assessed via a model selection approach in R v.4.2.1 (R Core Team, 2022). Candidate models of both baseline and stress-induced glucose included combinations of: 1) a fixed effect of the average of one weather variable (temperature, wind speed, or precipitation) over

one of two timescales (3 h before capture or 72 h before capture) as well as a fixed effect of life history substage (incubation, near-hatching, or mid-provisioning), 2) the weather variable, the life history substage and the interaction between them, and 3) mass and its interaction with life history substage (see Supplementary Tables S1 and S2 or full list of candidate models). All stress-induced glucose models also included baseline glucose as a covariate. Tree swallows in this study were also involved in other experiments, all of which took place following the initial incubation capture. To account for experimental treatments and repeated sampling within and across years, both treatment and individual swallow identity were included as random effects in all models. Because different treatments were used in each year, the random effect for treatment also captures overall variation in breeding conditions from year to year. Finally, each model set also included an intercept only model with just the random effects for comparison, as well as a model that included life history stage alone. Corrected Akaike Information Criterion (AICc) scores were used to identify which candidate models were best supported, given the data (Burnham and Anderson, 2004). All models within $2 \Delta\text{AICc}$ of the best supported model were considered to have received meaningful support, and were individually evaluated. A full list of candidate models and their results can be found in Supplementary Tables S1 and S2.

3. Results

From a total of 171 female tree swallows at 431 capture events, 431 baseline glucose and 339 stress-induced glucose samples were collected (baseline (mean \pm sd): 212.6 \pm 28.7 pg/dL; stress-induced: 244.1 \pm 38.2 pg/dL). The full distribution of data for baseline and stress-induced glucose at each life history substage are shown in Fig. 1. After controlling for baseline glucose, birds captured at the near-hatching and

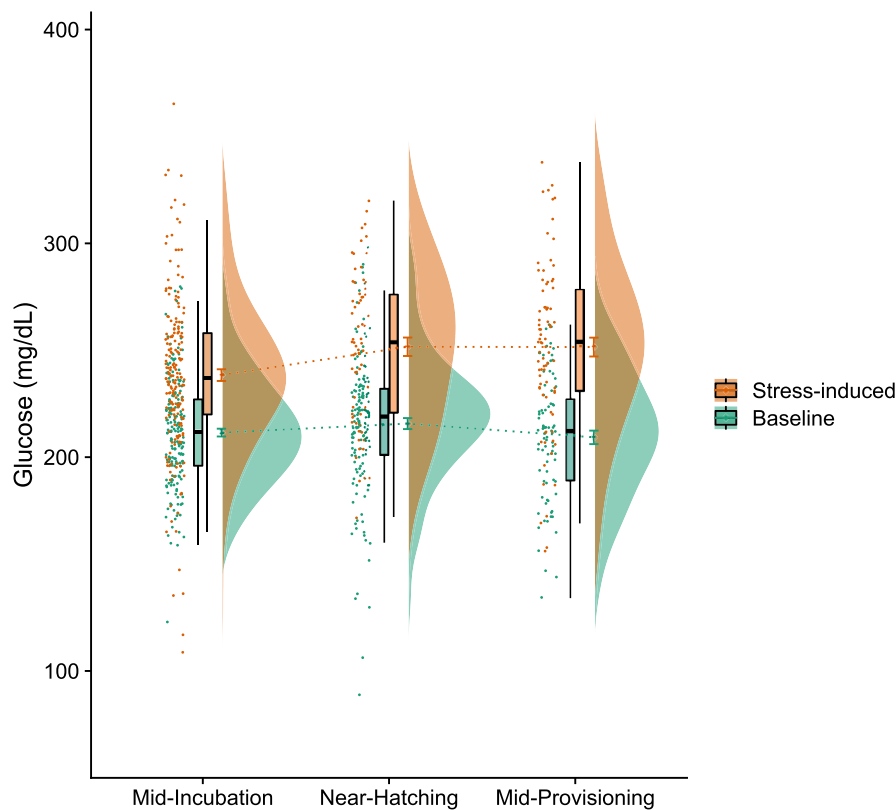


Fig. 1. Raincloud plot summarizing glucose data. From left to right for each life history substage: measured data points, a boxplot showing first quartile, median, and third quartile, standard error bars, and a bisected violin plot. Number of samples per capture event - mid-incubation: $n = 191$ baseline, $n = 191$ stress-induced; near-hatching: $n = 157$ baseline, $n = 64$ stress-induced; mid-provisioning: $n = 83$ baseline, $n = 79$ stress-induced.

mid-provisioning stages had higher stress-induced glucose (Fig. 1, Tables 2 and 3).

There was no support for a relationship between weather conditions and baseline glucose at either timescale. None of the candidate models received better support in predicting baseline glucose when compared with the null model (Supplementary Table S1).

In contrast, weather was retained in the best supported models of stress-induced glucose, where two models received similar support. The first included average ambient temperature during the 72 h before capture and the second included an interaction between precipitation during the 72 h before capture and the life history substage (Table 1; Supplementary Table S2). Both were a substantially better fit to the data than the intercept-only model (Supplementary Table S2; Δ AICc of 82.96 and 82.74). Female tree swallows that experienced colder temperatures on the three days preceding capture tended to mount a stronger glucose response to 30 min of restraint stress (Table 2, Fig. 2). The glucose response to rainfall in the three days preceding capture depended on breeding life history substage. Rain did not have a strong general effect, except during captures that occurred near hatching. During this life history substage, higher rain was associated with lower stress-induced glucose levels (Table 3, Fig. 3). Models that included average wind speed or body mass as a predictor were not supported (Supplementary Table S2; wind and mass models >4 Δ AICc). Models that included a 3-h timescale were not supported relative to models with a 72-h timescale as a predictor.

4. Discussion

Contrary to our predictions, birds did not alter baseline glucose levels or reduce stress-induced glucose levels in response to inclement weather and its associated food limitation. However, experiencing these conditions appeared to prime the metabolic stress response to a subsequent challenge. Specifically, adult tree swallows that experienced colder temperatures during the preceding seventy-two hours appeared to mount a higher glucose response to restraint stress than those that had recently experienced warmer temperatures. An increased responsiveness to a stressor following challenging conditions could be adaptive, if experiencing one challenge is indicative of an increased likelihood of encountering future challenges (Sapolsky et al., 2000; Romero et al., 2009; Boussaid-Om Ezzine et al., 2010; Del Giudice et al., 2018).

Many previous studies have shown that the glucose response to

stressors may be context dependent. Time since last meal or circadian patterns can explain the presence or absence of a glucose elevation following challenges (Widmaier and Kunz, 1993; Ramage-Healey and Romero, 2000). Condition-associated measures such as amount of visible fat or mass may also play a role in the degree of glucose elevation or its relationship to the concomitant rise in glucocorticoid levels (Malisch et al., 2018; Taff et al., 2022). Pygmy rattlesnakes, *Sistrurus miliarius*, appear to show increased glucose stress responses when their body temperature is higher (Kelley et al., 2021). Overall, our results demonstrate that the glucose stress response within a population of wild vertebrates also varies in accordance with exposure to a preceding challenge.

We initially expected that tree swallows experiencing cold temperatures, which decrease food abundance (Winkler et al., 2013), would mobilize less glucose in response to an acute stressor than birds experiencing more benign conditions. This prediction comes from our hypothesis that tree swallows already coping with resource limitation might not be capable of mounting a robust energetic response to an additional stressor. The opposite pattern that we observed instead likely stems from the role of glucose in preparing for and responding to challenges (Sapolsky et al., 2000). Stress-induced hyperglycemia is primarily a byproduct of reduced glucose uptake and does not provide additional energy during the initiation of and response to a challenge, but rather helps to restore energy reserves used up in the flight or fight response (Romero and Beattie, 2022). A heightened glucose response – that enables faster recovery in the hours and days following an acute stressor – experienced in an already challenging environment could be an adaptive way for organisms to better manage the energetic load of multiple sequential stressors. However, very few studies have tested this (but see Lankford et al., 2003). Furthermore, because the costs and benefits of glucose elevation vary across contexts, the adaptive value of the glucose stress response – and its stress-induced priming – are also likely to vary. For example, rufous-winged sparrows, *Peucaea carpalis*, exhibit a decrease in circulating glucose in response to stress during molt and during the non-breeding season (Deviche et al., 2016). It is also worth noting that while we interpret the increase in stress-induced glucose following inclement weather seen here to be adaptive it could also be costly, if individuals subsequently experience a stressor that does not increase energetic demand (and thus the need for glucose mobilization). Glucose responses to acute stress may also vary based on the organism's reserves of lipids and proteins, which may be preferentially utilized for

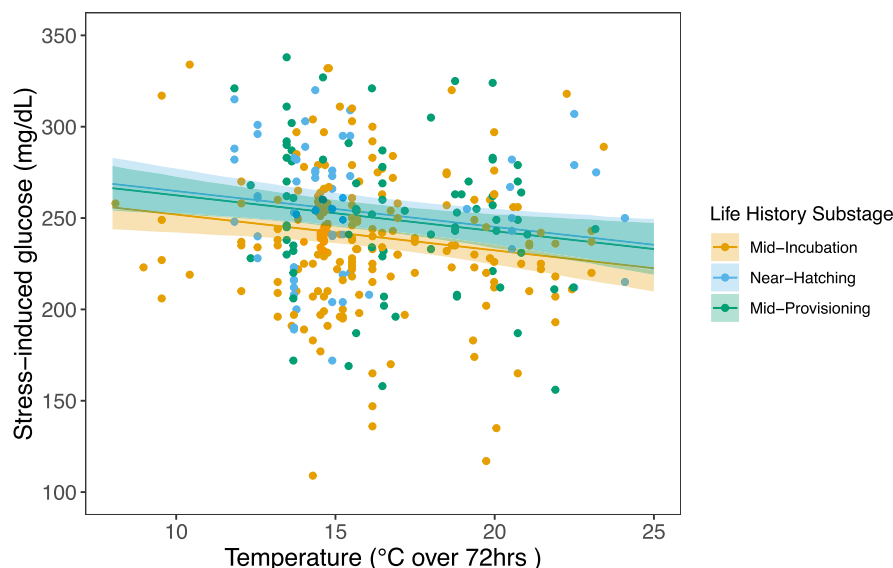


Fig. 2. The relationship between ambient temperature (average temperature over the 72 h before capture) and the glucose response to acute stress in female tree swallows. Points are measured glucose values. Lines and shaded regions are the predictions from the “72 h Temperature” model of stress-induced glucose.

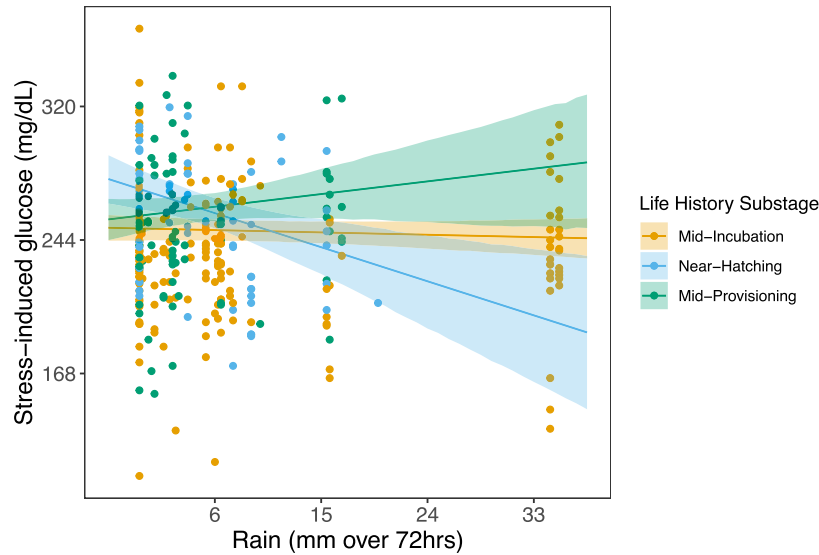


Fig. 3. The relationship between precipitation (average rainfall 3 days before capture) and the glucose response to acute stress in female tree swallows. Points are measured glucose values. Lines and shaded regions are the predictions from the “Rain(72 h)*LHS” model of stress-induced glucose.

Table 1

Top ranked models of stress-induced glucose. For comparison, the top performing models and the intercept with random effects only model are included. No other models were within 2 Δ AICc of the best supported models. K: number of parameters in the model, AICc: Corrected Akaike Information Criterion.

Stress-Induced Glucose Models	Log Likelihood	K	Δ AICc	Relative Likelihood	Weight
Temperature 72 h Before + Life history substage	-1669.98	6	0	1	0.29
Rain 72 h Before * Life History Substage	-1668.00	8	0.22	0.89	0.26
Intercept Only	-1715.57	2	82.96	0.00	0

Table 2

Summary of the top-ranked stress-induced glucose model: Shows model predictions with scaled continuous variables (stress-induced glucose, baseline glucose, temperature).

Coefficient	Estimate	S.E.	95% C.I.	p-value
Intercept	-0.17	0.16	-0.33, -0.01	0.041
Temperature 72 h Before	-0.11	0.12	-0.22, 0.01	0.070
Life history substage 2 (Near-Hatching)	0.32	0.28	0.04, 0.59	0.024
Life history substage 3 (Mid-Provision)	0.35	0.25	0.11, 0.60	<0.01
Baseline Glucose	0.28	0.11	0.17, 0.39	<0.001

energy in some taxa and during certain periods of the annual cycle, such as migration (Gerson and Guglielmo, 2011; Kuzmiak et al., 2012). Future work that tests the relationship between glucose responses and fitness would help in understanding glucose phenotypes in wild animals.

In contrast to prior literature, there was no relationship between baseline glucose levels and weather in breeding tree swallows. Studies in free-living mammals (Schradin et al., 2015) and captive birds (Montoya et al., 2018) have found that baseline glucose is negatively associated with temperature. However, baseline glucose can also be influenced by food availability in complex ways. In captivity, fasted birds typically have lower baseline glucose than non-fasted controls (Romero and Wingfield, 2016). But a similar pattern may not be seen during natural food limitation; for example, free-living tree swallows with lower mass have higher baseline glucose levels (Taff et al., 2022). Thus, when low

Table 3

Summary of second-ranked stress-induced glucose model: Shows model predictions with scaled continuous variables (stress-induced glucose, baseline glucose, rain).

Coefficient	Estimate	S.E.	95% C.I.	p-value
Intercept	-0.14	0.15	-0.29, 0.02	0.087
Rain 72 h Before	-0.03	0.10	-0.14, 0.07	0.503
Life History Substage 2 (Near-Hatching)	0.25	0.27	-0.02, 0.52	0.065
Life History Substage 3 (Mid-Provision)	0.35	0.25	0.10, 0.60	<0.01
Baseline Glucose	0.28	0.11	0.17, 0.39	<0.001
Rain 72 h Before * Life History Substage 2	-0.48	0.39	-0.87, -0.08	0.02
Rain 72 h Before * Life History Substage 3	0.22	0.36	-0.13, 0.58	0.212

ambient temperatures are coupled with low food availability, as they are for tree swallows, opposing effects of temperature and food availability on baseline glucose could mask relationships with either of these factors considered individually. In many previous studies that have found an association between baseline glucose and temperature, temperature and food availability varied independently, or were negatively correlated (Schradin et al., 2015; Gangloff et al., 2016; Montoya et al., 2018).

Another possibility is that a lack of a relationship between ambient temperature and baseline glucose may simply reflect a well-attuned energetic maintenance to this specific labile perturbation factor (Wingfield et al., 1998). Considering that baseline glucose is also tied to pace of life across other species, perhaps glucose levels are tightly regulated and not expected to vary considerably unless an emergency life history stage is triggered (Wingfield et al., 1998; Tomasek et al., 2019). However, this is an unlikely explanation for the lack of a baseline glucose-temperature relationship as tree swallows in this population exhibit low repeatability of baseline glucose (Taff et al., 2022). One unique difference between birds and other vertebrates is that birds maintain significantly higher circulating glucose (Sweazea, 2022). This suggests the possibility that birds may suffer fewer costs of high glucose levels (Ku and Sohal, 1993; Cohen et al., 2007; Braun and Sweazea, 2008). However, there is evidence that high glucose levels can be costly in birds, and that glucose regulation entails life history trade-offs. For example, increased glycated hemoglobin—a byproduct of high circulating glucose—among older collared flycatchers (*Ficedula albicollis*) is

correlated with a lower likelihood to return to the breeding site the following year (Récapet et al., 2016). In captive zebra finches (*Taeniopygia guttata*), challenging developmental (large brood size during rearing) and adult (high foraging cost) environments lead to high baseline glucose levels in adulthood and shorter lifespans (Montoya et al., 2018). It is worth noting, however, that these patterns could reflect individuals increasing baseline glucose as an adaptive response to mobilize energy in challenging conditions, rather than a direct cost of glucose elevation. Future work should explore how various life history constraints and challenging conditions influence how organisms regulate baseline glucose levels in complex natural environments.

We also found that temperature was a better general predictor of stress-induced glucose than wind speed or precipitation. This pattern is consistent with the idea that temperature is the primary environmental driver of food availability in our study population (Winkler et al., 2013). However, rainfall around the time of hatching – but not during other sampling periods – was also associated with lower stress-induced glucose levels. In other populations of tree swallows, precipitation over the past three days is associated with declines in nestling mass, likely due to a temporary decline in food availability, and a compensatory increase in female foraging behavior (Cox et al., 2019). The ultimate effect of precipitation on tree swallow behavior and fitness may depend on whether it is experienced during warm or cold conditions (Garrett et al., 2022). Periods of food limitation that occur during the peak period of nestling provisioning are likely to represent the greatest overall energetic challenge, as well as the greatest fitness cost (Shipley et al., 2020). Thus, it is unclear why tree swallows appear to be modulating their glucose response to stress in response to precipitation around the time of hatching but not during the nestling provisioning (or mid-incubation) periods. Also of note is that birds with higher baseline glucose levels had higher stress-induced glucose. Therefore, while baseline glucose itself was not associated with prevailing weather conditions, it is still an important component of the overall energetic response to stressful conditions through its effects on the initial glucose set point.

The dynamics of various mediators of the stress response, and its general flexibility, are important and understudied aspects of stress biology (Breuner et al., 2013; Taff and Vitousek, 2016). Our results in tree swallows suggest that the glucose response may be subject to priming under stressful conditions. This is consistent with findings that previous challenges influence glucocorticoid regulation in response to future challenges, both in tree swallows (Taff et al., 2018; Vitousek et al., 2022) and many other organisms (e.g., Dallman, 2007; Cyr and Romero, 2007; Lattin and Romero, 2014; Krause et al., 2018). That both glucose and corticosterone show a similar priming effect in this species (Vitousek et al., 2022) is especially interesting because these patterns appear not to result from a causal effect of corticosterone on glucose (Taff et al., 2022). This could instead be the result of independent upregulation of different components of the acute stress response during challenging environmental conditions. It is also possible that glucose responses to stress are one aspect of a suite of co-regulated traits whose responses to future challenges are primed by exposure to an initial challenge (Gormally and Romero, 2020). Overall, we suggest that the priming of different components of the stress response may be an underappreciated aspect of how organisms respond to capricious environments. More studies are needed to assess these effects, and determine how they vary based on prior experiences and the level and nature of threats.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cbpa.2023.111419>.

Funding

This work was supported by funding in the form of grants awarded to MV from the National Science Foundation (IOS-1457251), DARPA (D17AP00033), and USDA-NIFA Hatch (1017321).

Declaration of Competing Interest

The authors declare no conflict of interest.

Data availability

Data will be made available on request.

Acknowledgements

The authors thank the many students and research assistants who helped collect the field data, including L Liu, G Levesque, A Pinals, J Colcombe, V Rodriguez-Arcilla, G Lopez, D Myskiw, O Maurelli, A Yrizarry-Medina, D Lee, J Yeung, A Fox, B Johnson, A Rodriguez, J Strouse, K Tannis, R Kochmaruk, J Collison, A Anker, C Kallenberg, A Dopkin, and, especially, D Scheck. We further thank C Miller, S McNew, and M Pipkin for their thoughts on the paper through various lab meetings. Special thanks to J Uehling, J Houtz, D Chang Van Oordt, and A Injaian for their help with both field work and their thoughts on the development of the paper.

Statement on Animal Safety.

All protocols and procedures were approved by Cornell University's IACUC (2019-0023), and conducted under appropriate state and federal permits.

References

- Akiba, Y., Chida, Y., Takahashi, T., Ohtomo, Y., Sato, K., Takahashi, K., 1999. Persistent hypoglycemia induced by continuous insulin infusion in broiler chickens. *Br. Poult. Sci.* 40, 701–705. <https://doi.org/10.1080/00071669987124>.
- Boonstra, R., Hik, D., Singleton, G.R., Tinnikov, A., 1998. The impact of predator-induced stress on the snowshoe hare cycle. *Ecol. Monogr.* 68, 371–394. [https://doi.org/10.1890/0012-9615\(1998\)068\[0371:TIOPIS\]2.0.CO;2](https://doi.org/10.1890/0012-9615(1998)068[0371:TIOPIS]2.0.CO;2).
- Boussaid-Om Ezzine, S., Everaert, N., Métayer-Coustard, S., Rideau, N., Berri, C., Joubert, R., Temim, S., Collin, A., Tesseraud, S., 2010. Effects of heat exposure on Akt/S6K1 signaling and expression of genes related to protein and energy metabolism in chicken (*Gallus gallus*) pectoralis major muscle. *Comp. Biochem. Physiol. B: Biochem. Mol. Biol.* 157, 281–287. <https://doi.org/10.1016/j.cbpb.2010.07.001>.
- Braun, E.J., Sweazea, K.L., 2008. Glucose regulation in birds. *Comp. Biochem. Physiol. B: Biochem. Mol. Biol.* 151, 1–9. <https://doi.org/10.1016/j.cbpb.2008.05.007>.
- Breuner, C.W., Delehanty, B., Boonstra, R., 2013. Evaluating stress in natural populations of vertebrates: total CORT is not good enough. *Funct. Ecol.* 27, 24–36. <https://doi.org/10.1111/1365-2435.12016>.
- Burnham, K.P., Anderson, D.R., 2004. Multimodel inference: understanding AIC and BIC in model selection. *Sociol. Methods Res.* 33 (2), 261–304.
- Busch, D.S., Sperry, T.S., Wingfield, J.C., Boyd, E.H., 2008. Effects of repeated, short-term, corticosterone administration on the hypothalamo-pituitary-adrenal axis of the white-crowned sparrow (*Zonotrichia leucophrys gambelii*). *Gen. Comp. Endocrinol.* 158, 211–223. <https://doi.org/10.1016/j.ygcen.2008.06.004>.
- Carragher, J.F., Rees, C.M., 1994. Primary and secondary stress responses in golden perch, *Macquaria ambigua*. *Comp. Biochem. Physiol. A Physiol.* 107, 49–56. [https://doi.org/10.1016/0300-9629\(94\)90272-0](https://doi.org/10.1016/0300-9629(94)90272-0).
- Cohen, A., Klasing, K., Ricklefs, R., 2007. Measuring circulating antioxidants in wild birds. *Comp. Biochem. Physiol. B: Biochem. Mol. Biol.* 147, 110–121. <https://doi.org/10.1016/j.cbpb.2006.12.015>.
- Cox, Amelia R., Robertson, Raleigh J., Lendvai, Adam Z., Kennedy, Everitt, Frances, Bonier, 2019. Rainy springs linked to poor nestling growth in a declining avian aerial insectivore (*Tachycineta bicolor*). *Proc. R. Soc. B Biol. Sci.* 286, 20190018. <https://doi.org/10.1098/rspb.2019.0018>.
- Cyr, N.E., Romero, M.L., 2007. Chronic stress in free-living European starlings reduces corticosterone concentrations and reproductive success. *Gen. Comp. Endocrinol.* 151, 82–89. <https://doi.org/10.1016/j.ygcen.2006.12.003>.
- Dallman, M.F., 2007. Modulation of stress responses: how we cope with excess glucocorticoids. *Exp. Neurol.* 206, 179–182. <https://doi.org/10.1016/j.expneurol.2007.06.002>.
- Dallman, M.F., Bhatnagar, S., 2011. Chronic stress and energy balance: Role of the hypothalamo-pituitary-adrenal axis. In: *Comprehensive Physiology*. John Wiley & Sons, Ltd, pp. 179–210. <https://doi.org/10.1002/cphy.cp070410>.
- Dallman, M.F., Strack, A.M., Akana, S.F., Bradbury, M.J., Hanson, E.S., Scribner, K.A., Smith, M., 1993. Feast and famine: critical role of glucocorticoids with insulin in daily energy flow. *Front. Neuroendocrinol.* 14, 303–347. <https://doi.org/10.1006/frne.1993.1010>.
- Davies, A.O., Lefkowitz, R.J., 1984. Regulation of β -adrenergic receptors by steroid hormones. *Annu. Rev. Physiol.* 46, 119–130. <https://doi.org/10.1146/annurev.ph.46.030184.001003>.

- Del Giudice, M., Buck, C.L., Chaby, L.E., Gormally, B.M., Taff, C.C., Thawley, C.J., Vitousek, M.N., Wada, H., 2018. What is stress? A systems perspective. *Integr. Comp. Biol.* 58, 1019–1032. <https://doi.org/10.1093/icb/icy114>.
- Deviche, P., Valle, S., Gao, S., Davies, S., Bittner, S., Carpentier, E., 2016. The seasonal glucocorticoid response of male Rufous-winged Sparrows to acute stress correlates with changes in plasma uric acid, but neither glucose nor testosterone. *Gen. Comp. Endocrinol.* 235, 78–88. <https://doi.org/10.1016/j.ygcen.2016.06.011>.
- Fokidis, H.B., Hurley, L., Rogowski, C., Sweazea, K., Deviche, P., 2011. Effects of captivity and body condition on plasma corticosterone, locomotor behavior, and plasma metabolites in curve-billed thrashers. *Physiol. Biochem. Zool.* 84, 595–606. <https://doi.org/10.1086/662068>.
- Gangloff, E.J., Holden, K.G., Telemeco, R.S., Baumgard, L.H., Bronikowski, A.M., 2016. Hormonal and metabolic responses to upper temperature extremes in divergent life-history ecotypes of a garter snake. *J. Exp. Biol.* 219, 2944–2954. <https://doi.org/10.1242/jeb.143107>.
- Garrett, D.R., Pelletier, F., Garant, D., Bélisle, M., 2022. Interacting effects of cold snaps, rain, and agriculture on the fledging success of a declining aerial insectivore. *Ecol. Appl.* 32, e2645 <https://doi.org/10.1002/eap.2645>.
- Gerson, A.R., Guglielmo, C.G., 2011. Flight at low ambient humidity increases protein catabolism in migratory birds. *Science*. 333 (6048), 1434–1436. <https://doi.org/10.1126/science.1210449>.
- Gormally, B.M.G., Romero, L.M., 2020. What are you actually measuring? A review of techniques that integrate the stress response on distinct time-scales. *Funct. Ecol.* 34, 2030–2044. <https://doi.org/10.1111/1365-2435.13648>.
- Hik, D.S., McColl, C.J., Boonstra, R., 2001. Why are Arctic ground squirrels more stressed in the boreal forest than in alpine meadows? *Écoscience* 8, 275–288. <https://doi.org/10.1080/11956860.2001.11682654>.
- Hilker, M., Schwachtje, J., Baier, M., Balazadeh, S., Bäurle, I., Geiselhardt, S., Hincha, D. K., Kunze, R., Mueller-Roebber, B., Rillig, M.C., Rolff, J., Romeis, T., Schmillig, T., Steppuhn, A., van Dongen, J., Whitchcomb, S.J., Wurst, S., Zuther, E., Kopka, J., 2016. Priming and memory of stress responses in organisms lacking a nervous system. *Biol. Rev.* 91, 1118–1133. <https://doi.org/10.1111/brv.12215>.
- Imlay, T., Mann, H., Leonard, M., 2017. No effect of insect abundance on nestling survival or mass for three aerial insectivores. *Avian Conservation and Ecology* 12. <https://doi.org/10.5751/ACE-01092-120219>.
- Irons, R.D., Harding Scurr, A., Rose, A.P., Hagelin, J.C., Blake, T., Doak, D.F., 2017. Wind and rain are the primary climate factors driving changing phenology of an aerial insectivore. *Proc. R. Soc. B Biol. Sci.* 284, 20170412. <https://doi.org/10.1098/rspb.2017.0412>.
- Jeronen, E., Isometsä, P., Hissa, R., Pyörnilä, A., 1976. Effect of acute temperature stress on the plasma catecholamine, corticosterone and metabolite levels in the pigeon. *Comp. Biochem. Physiol. C Comp. Pharmacol.* 55, 17–22. [https://doi.org/10.1016/0306-4492\(76\)90005-8](https://doi.org/10.1016/0306-4492(76)90005-8).
- Jessop, T.S., Tucker, A.D., Limpus, C.J., Whittier, J.M., 2003. Interactions between ecology, demography, capture stress, and profiles of corticosterone and glucose in a free-living population of Australian freshwater crocodiles. *Gen. Comp. Endocrinol.* 132, 161–170. [https://doi.org/10.1016/S0016-6480\(03\)00078-9](https://doi.org/10.1016/S0016-6480(03)00078-9).
- Kelley, S., Farrell, T.M., Lind, C.M., 2021. Validating the use of a quick-read glucometer to assess the glycemic response to short-term capture stress in two species of snake. In: *Nerodia sipedon and Sistrurus miliarius*. *COPE* 109, pp. 436–442. <https://doi.org/10.1643/h2020102>.
- Krause, J.S., Pérez, J.H., Chmura, H.E., Meddle, S.L., Hunt, K.E., Gough, L., Boelman, N., Wingfield, J.C., 2018. Weathering the storm: do arctic blizzards cause repeatable changes in stress physiology and body condition in breeding songbirds? *Gen. Comp. Endocrinol.* 267, 183–192. <https://doi.org/10.1016/j.ygcen.2018.07.004>.
- Ku, H.-H., Sohal, R.S., 1993. Comparison of mitochondrial pro-oxidant generation and anti-oxidant defenses between rat and pigeon: possible basis of variation in longevity and metabolic potential. *Mech. Ageing Dev.* 72, 67–76. [https://doi.org/10.1016/0047-6374\(93\)90132-B](https://doi.org/10.1016/0047-6374(93)90132-B).
- Kuzmiak, S., Glancy, B., Sweazea, K.L., Willis, W.T., 2012. Mitochondrial function in sparrow pectoralis muscle. *J. Exp. Biol.* 215, 2039–2050. <https://doi.org/10.1242/jeb.065094>.
- Lankford, S.E., Adams, T.E., Cech Jr., J.J., 2003. Time of day and water temperature modify the physiological stress response in green sturgeon, *Acipenser medirostris*. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.* 135, 291–302. [https://doi.org/10.1016/S1095-6433\(03\)00075-8](https://doi.org/10.1016/S1095-6433(03)00075-8).
- Lattin, C.R., Romero, L.M., 2014. Chronic stress alters concentrations of corticosterone receptors in a tissue-specific manner in wild house sparrows (*Passer domesticus*). *J. Exp. Biol.* 217, 2601–2608. <https://doi.org/10.1242/jeb.103788>.
- Malisch, J.L., Bennett, D.J., Davidson, B.A., Wenker, E.E., Suzich, R.N., Johnson, E.E., 2018. Stress-induced hyperglycemia in white-throated and white-crowned sparrows: a new technique for rapid glucose measurement in the field. *Physiol. Biochem. Zool.* 91, 943–949. <https://doi.org/10.1086/698536>.
- Malko, K., Mentasana, L., Casagrande, S., Hau, M., 2022. Quantifying glucocorticoid plasticity using reaction norm approaches: there still is so much to discover! *Integr. Comp. Biol.* 62, 58–70. <https://doi.org/10.1093/icb/icy196>.
- McGuinness, O.P., Fujiwara, T., Murrell, S., Bracy, D., Neal, D., O'Connor, D., Cherrington, A.D., 1993. Impact of chronic stress hormone infusion on hepatic carbohydrate metabolism in the conscious dog. *American Journal of Physiology-Endocrinology and Metabolism* 265, E314–E322. <https://doi.org/10.1152/ajpendo.1993.265.2.E314>.
- Montoya, B., Briga, M., Jimeno, B., Moonen, S., Verhulst, S., 2018. Baseline glucose level is an individual trait that is negatively associated with lifespan and increases due to adverse environmental conditions during development and adulthood. *J. Comp. Physiol. B*. 188, 517–526. <https://doi.org/10.1007/s00360-017-1143-0>.
- Munck, A., 1971. Glucocorticoid inhibition of glucose uptake by peripheral tissues: old and new evidence, molecular mechanisms, and physiological significance. *Perspect. Biol. Med.* 14, 265–289. <https://doi.org/10.1353/pbm.1971.0002>.
- Neuman-Lee, L.A., Hudson, S.B., Webb, A.C., French, S.S., 2019. Investigating the relationship between corticosterone and glucose in a reptile. *J. Exp. Biol.* <https://doi.org/10.1242/jeb.203885>.
- Ouyang, J.Q., Lendvai, Á., Dakin, R., Domalik, A.D., Fasanello, V.J., Vassallo, B.G., Haussmann, M.F., Moore, I.T., Bonier, F., 2015. Weathering the storm: parental effort and experimental manipulation of stress hormones predict brood survival. *BMC Evol. Biol.* 15, 1–8. <https://doi.org/10.1186/s12862-015-0497-8>.
- R Core Team, 2022. *R: A Language and Environment for Statistical Computing*.
- Récapet, C., Sibeaux, A., Cauchard, L., Doligez, B., Bize, P., 2016. Selective disappearance of individuals with high levels of glycated haemoglobin in a free-living bird. *Biol. Lett.* 12, 20160243. <https://doi.org/10.1098/rsbl.2016.0243>.
- Remage-Healey, L., Romero, L.M., 2000. Daily and seasonal variation in response to stress in captive starlings (*Sturnus vulgaris*): glucose. *Gen. Comp. Endocrinol.* 119, 60–68. <https://doi.org/10.1006/genen.2000.7492>.
- Romero, L.M., 2004. Physiological stress in ecology: lessons from biomedical research. *Trends Ecol. Evol.* 19, 249–255. <https://doi.org/10.1016/j.tree.2004.03.008>.
- Romero, L.M., Beattie, U.K., 2022. Common myths of glucocorticoid function in ecology and conservation. *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology* 337, 7–14.
- Romero, L.M., Wingfield, J.C., 2016. *Tempests, Poxes, Predators, and People: Stress in Wild Animals and how they Cope*. Oxford University Press, New York, NY, US.
- Romero, L.M., Dickens, M.J., Cyr, N.E., 2009. The reactive scope model — a new model integrating homeostasis, allostasis, and stress. *Horm. Behav.* 55, 375–389. <https://doi.org/10.1016/j.yhbeh.2008.12.009>.
- Sadoul, B., Leguen, I., Colson, V., Friggens, N.C., Prunet, P., 2015. A multivariate analysis using physiology and behavior to characterize robustness in two isogenic lines of rainbow trout exposed to a confinement stress. *Physiol. Behav.* 140, 139–147. <https://doi.org/10.1016/j.physbeh.2014.12.006>.
- Sapolsky, R.M., Romero, L.M., Munck, A.U., 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr. Rev.* 21, 55–89. <https://doi.org/10.1210/edrv.21.1.0389>.
- Scanes, C.G., Braun, E., 2013. Avian metabolism: its control and evolution. *Front. Biol.* 8, 134–159. <https://doi.org/10.1007/s11515-012-1206-2>.
- Schradin, C., Pillay, N., Kondratyeva, A., Yuen, C.-H., Schoepf, I., Krackow, S., 2015. Basal blood glucose concentration in free-living striped mice is influenced by food availability, ambient temperature and social tactic. *Biol. Lett.* 11, 20150208. <https://doi.org/10.1098/rsbl.2015.0208>.
- Shipley, J.R., Twining, C.W., Taff, C.C., Vitousek, M.N., Flack, A., Winkler, D.W., 2020. Birds advancing lay dates with warming springs face greater risk of chick mortality. *Proc. Natl. Acad. Sci.* 117, 25590–25594. <https://doi.org/10.1073/pnas.2009864117>.
- Smith, C.L., Toomey, M., Walker, B.R., Braun, E.J., Wolf, B.O., McGraw, K., Sweazea, K. L., 2011. Naturally high plasma glucose levels in mourning doves (*Zenaidura macroura*) do not lead to high levels of reactive oxygen species in the vasculature. *Zoology* 114, 171–176. <https://doi.org/10.1016/j.zool.2010.12.001>.
- Sweazea, K.L., 2022. Revisiting glucose regulation in birds – a negative model of diabetes complications. *Comp. Biochem. Physiol. B: Biochem. Mol. Biol.* 262, 110778 <https://doi.org/10.1016/j.cbpb.2022.110778>.
- Taff, C.C., Vitousek, M.N., 2016. Endocrine flexibility: optimizing phenotypes in a dynamic world? *Trends Ecol. Evol.* 31, 476–488. <https://doi.org/10.1016/j.tree.2016.03.005>.
- Taff, C.C., Zimmer, C., Vitousek, M.N., 2018. Efficacy of negative feedback in the HPA axis predicts recovery from acute challenges. *Biol. Lett.* 14, 20180131. <https://doi.org/10.1098/rsbl.2018.0131>.
- Taff, C.C., Zimmer, C., Scheck, D., Ryan, T.A., Houtz, J.L., Smees, M.R., Hendry, T.A., Vitousek, M.N., 2021. Plumage manipulation alters associations between behaviour, physiology, the internal microbiome and fitness. *Anim. Behav.* 178, 11–36. <https://doi.org/10.1016/j.anbehav.2021.05.012>.
- Taff, C.C., Zimmer, C., Ryan, T.A., van Oordt, D.C., Aborn, D.A., Ardia, D.R., Johnson, L. S., Rose, A.P., Vitousek, M.N., 2022. Individual variation in natural or manipulated corticosterone does not covary with circulating glucose in a wild bird. *J. Exp. Biol.* 225, jeb243262. <https://doi.org/10.1242/jeb.243262>.
- Thurston, R.J., Bryant, C.C., Korn, N., 1993. The effects of corticosterone and catecholamine infusion on plasma glucose levels in chicken (*Gallus domesticus*) and Turkey (*Meleagris gallapavo*). *Comp. Biochem. Physiol. C: Pharmacol. Toxicol. Endocrinol.* 106, 59–62. [https://doi.org/10.1016/0742-8413\(93\)90254-I](https://doi.org/10.1016/0742-8413(93)90254-I).
- Tomasek, O., Bobek, L., Kralova, T., Adamkova, M., Albrecht, T., 2019. Fuel for the pace of life: baseline blood glucose concentration co-evolves with life-history traits in songbirds. *Funct. Ecol.* 33, 239–249. <https://doi.org/10.1111/1365-2435.13238>.
- Tomášek, O., Bobek, L., Kauzálková, T., Kauzál, O., Adamková, M., Horák, K., Kumar, S. A., Maniava, J.P., Munclinger, P., Nana, E.D., Nguetefack, T.B., Sedláček, O., Albrecht, T., 2022. Latitudinal but not elevational variation in blood glucose level is linked to life history across passerine birds. <https://doi.org/10.32942/osf.io/b793g>.
- Vitousek, M.N., Houtz, J.L., Pipkin, M.A., Chang van Oordt, D.A., Hallinger, K.K., Uehling, J.J., Zimmer, C., Taff, C.C., 2022. Natural and experimental cold exposure in adulthood increase the sensitivity to future stressors in a free-living songbird. *Funct. Ecol.* 36, 2531–2543. <https://doi.org/10.1111/1365-2435.14144>.
- Weber, J.-M., 2011. Metabolic fuels: regulating fluxes to select mix. *J. Exp. Biol.* 214, 286–294. <https://doi.org/10.1242/jeb.047050>.
- Widmaier, E.P., Kunz, T.H., 1993. Basal, diurnal, and stress-induced levels of glucose and glucocorticoids in captive bats. *J. Exp. Zool.* 265, 533–540. <https://doi.org/10.1002/jez.1402650509>.

- Wingfield, J.C., 2005. The concept of Allostasis: coping with a capricious environment. *J. Mammal.* 86, 248–254. <https://doi.org/10.1644/BHE-004.1>.
- Wingfield, J.C., Romero, L.M., 2011. Adrenocortical responses to stress and their modulation in free-living vertebrates. In: Terjung, R. (Ed.), *Comprehensive Physiology*. <https://doi.org/10.1002/cphy.cp070411>.
- Wingfield, J.C., Sapolsky, R.M., 2003. Reproduction and resistance to stress: when and how. *J. Neuroendocrinol.* 15, 711–724. <https://doi.org/10.1046/j.1365-2826.2003.01033.x>.
- Wingfield, J.C., Maney, D.L., Breuner, C.W., Jacobs, J.D., Lynn, S., Ramenofsky, M., Richardson, R.D., 1998. Ecological Bases of Hormone—Behavior Interactions: The “Emergency Life History Stage.”. *Am. Zool.* 38, 191–206. <https://doi.org/10.1093/icb/38.1.191>.
- Winkler, D.W., Luo, M.K., Rakhimberdiev, E., 2013. Temperature effects on food supply and chick mortality in tree swallows (*Tachycineta bicolor*). *Oecologia* 173, 129–138. <https://doi.org/10.1007/s00442-013-2605-z>.