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Post-natal corticosterone exposure downregulates the HPA axis through adulthood in a common passerine

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ABSTRACT

The hypothalamic–pituitaryadrenal (HPA) axis is one of the most important physiological mechanisms for mediating life-history trade-offs by reallocating resources to immediate survival from other life-history components during a perturbation. Early-life stressor experience and associated upregulation of glucocorticoids can induce short- and long-term changes to the HPA axis in ways that may optimize survival and/or reproduction for the expected adult environment. Although short-term changes to the HPA axis following perinatal stress are well documented, we know less about the long-term effects of early-life stress especially for non-mammalian wild species. Here, we determined long-term effects of experimental post-natal increases in a circulating glucocorticoid on the HPA axis in a common passerine bird, the house sparrow (*Passer domesticus*). We manipulated circulating corticosterone in wild, free-living nestlings, transferred fledglings to captivity and assessed corticosterone response to a standardized capture-restraint protocol at the pre-fledging, juvenile, and adult stages. Early-life corticosterone manipulation was associated with depressed baseline and stress-induced concentrations of corticosterone at all stages of life, through adulthood. These results provide rare evidence for the effects of early-life stressor experiences through adulthood, with important implications for understanding developmental programming of an endocrine mediator of life history trade-offs.

1. Introduction

The environment an animal experiences during growth and maturation interacts with the genotype to guide the development of the phenotype (Monaghan, 2008). In vertebrates, it is well established that steroid hormones can have organizational (i.e. "programming") effects on physiology and behavior (Arnold and Breedlove, 1985) and that the perinatal period is a critical period in which these long-term changes can occur (Adkins-Regan et al., 1994; Arnold and Breedlove, 1985). The field of programming effects was historically associated mainly with so-called "sex hormones", but has expanded in recent decades to include other early-life hormone exposure events, such as glucocorticoid (GC) upregulation associated with stress (Cottrell and Seckl, 2009; Welberg and Seckl, 2001). Understanding phenotypic effects of early-life stressor experiences on both short- and long-term scales has broad implications for animal husbandry, welfare, and conservation (Goerlich et al., 2012).

Early-life stressor experiences are associated with long-term changes in neurology (Lucassen et al., 2013; Welberg and Seckl, 2001), physiology (Cottrell and Seckl, 2009; Matthews, 2002) and behavior (Seckl, 2004). Studies of captive rodents and birds, and at least one wild bird demonstrate that early-life stressor experiences induce changes to the GC stress response of juveniles and young adults (e.g., Banerjee et al., 2012; Grace and Anderson, 2018; Kalinichev et al., 2002; Liu et al., 2000; Marasco et al., 2012; Pravosudov and Kitaysky, 2006; Schmidt et al., 2014; Slotten et al., 2006; Spencer et al., 2009), and behavioral traits including neophobia, anxiety, and aggression (Boccia and Pedersen, 2001; Durand et al., 1998; Kalinichev et al., 2002; Spencer and Verhulst, 2007), as well as other physiological (e.g., telomere attrition (Angelier et al., 2017)), behavioral (e.g., foraging behavior and cognitive ability (Kitaysky et al., 2003)), and life history traits (Drummond and Ancona, 2015; Lindström, 1999) (reviewed in Schoech et al., 2011). Following high early-life stressor experience or GC manipulation, zebra finches (*Taeniopygia guttata*), western scrub jays (*Aphelocoma californica*), male Nazca boobies (*Sula granti*), and male laboratory rodents, among other species display a hypersensitivity of the hypothalamic–pituitaryadrenal (HPA) axis response to stressors (Grace and Anderson, 2018; Kalinichev et al., 2002; Pravosudov and Kitaysky, 2006; Schoech et al., 2011; Spencer et al., 2009), but no change in circulating baseline corticosterone (CORT, the primary avian glucocorticoid) concentration (Grace and Anderson, 2018; Pravosudov

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and Kitaysky, 2006; Schoech et al., 2011; Spencer et al., 2009). However, opposite effects, or no effect have been found in a growing number of studies, suggesting that results can be species- and sex-specific, and dependent on stressor intensity, type, and period of exposure (Matthews, 2002). For example and in contrast to the above results for males, early-life stressor experience induces no hypersensitivity and a decrease in baseline CORT concentration ([CORT]) in female Nazca boobies and female laboratory rats (Grace and Anderson, 2018; Slotten et al., 2006). European starlings (*Sturnus vulgaris*) of both sexes display juvenile downregulation of the GC stress response following pre-natal GC exposure (Love and Williams, 2008a), and post-natal GC exposure is associated with increased baseline [CORT] in a separate study of zebra finches (Crino et al., 2014), and no change to the restraint-induced GC stress response in song sparrows (*Melospiza melodia*) (Schmidt et al., 2014). In Japanese quail (*Coturnix coturnix japonica*) of both sexes, pre-natal GC elevation is associated with a shortened GC stress response in one study (Zimmer et al., 2013), but no change to the GC stress response in another (Marasco et al., 2012), while post-natal GC exposure resulted in sex-specific HPA axis changes (Marasco et al., 2012). Thus, there remains considerable lack of consensus regarding long-term effects of early stressor exposure on the GC stress response. Additionally, while there is abundant evidence of short-term effects of early-life stressors on the HPA axis, researchers rarely follow subjects to adulthood (Crino et al., 2014; Marasco et al., 2012; Pakkala et al., 2016), especially for wild species (Drummond and Ancona, 2015; but see Grace and Anderson, 2018; Lendvai et al., 2009; Schmidt et al., 2014), casting doubt on the persistence of these effects.

GCs are of special interest in the field of organizational effects because of their role in determining individual fitness, both at baseline and stress-induced levels. At baseline levels, GCs play a fundamental role in energy allocation in response to predictable life-history events (Crespi et al., 2013; McEwen and Wingfield, 2003). Thus, baseline GC levels are expected to correlate with energetic demands associated with life-history stage, circadian patterns of foraging, and seasonal activities (reviewed in Crespi et al., 2013; McEwen and Wingfield, 2003; Sapolsky et al., 2000). At stress-induced levels, the primary function of the GCs are to mediate rapid behavioral and physiological responses to perceived threats to homeostasis (Sapolsky et al., 2000), thus promoting immediate survival and facilitating response to unpredictable environmental factors (i.e., "labile perturbation factors"; Wingfield et al., 1998). This response is flexible and can be modulated to balance benefits to immediate survival against long-term fitness costs of elevated GCs (Angelier and Wingfield, 2013; Wingfield and Sapolsky, 2003). Thus, the GC stress response is one of the most important physiological mechanisms that mediates life-history trade-offs by re-allocating resources to immediate survival from other life-history components (Angelier et al., 2013; Crespi et al., 2013; Wingfield and Sapolsky, 2003).

In recent years, the historically negative view of developmental stress has shifted to focus on its potentially beneficial programming effects (Crino and Breuner, 2015; Gluckman et al., 2007; Love and Williams, 2008b; Monaghan, 2008). Early life stressors may be important indicators of future environmental conditions and associated organizational effects may work to match the phenotype to this predicted future environment ("Match-Mismatch Hypothesis"), (Crino and Breuner, 2015; Gluckman et al., 2007; Love and Williams, 2008b). These organizational effects can include long-term modifications to baseline GCs and the GC stress response, which may facilitate phenotypic matching by mediating life history tradeoffs between, for instance, survival and reproduction (Bókony et al., 2009; Crespi et al., 2013; Crino et al., 2014; Crino and Breuner, 2015), especially during unpredictable environmental perturbations. Under this hypothesis, adverse consequences of early-life programming occur when there is a mistmatch between the anticipated and actual mature environments (Gluckman et al., 2007; Nederhof and Schmidt, 2012).

Altricial birds have emerged as useful models to study the effects of post-natal glucocorticoid exposure because they lack a physiological link between mothers and offspring (i.e., maternal lactation) making it easier to disentangle postnatal maternal effects and endogenous effects in offspring, compared with mammalian studies (Spencer et al., 2009). Many avian studies of early-life stressor experience have focused on the effects of nutritional stress, caused either by directly manipulating food availability, or altering within-brood competition (Goerlich et al., 2012). This approach, however, makes it difficult to disentangle stressor experience from the confounding effects of competitive interactions, parental care, and changes in energetic resources. Here, we investigate long-term effects of early-life glucocorticoid exposure on the HPA axis stress response in a common bird species, the house sparrow (*Passer domesticus*). We experimentally elevate circulating [CORT] in wild, free-living house sparrow nestlings and measure baseline and stress-induced circulating [CORT] in captivity through adulthood. Under the Match-Mismatch hypothesis, we predict that elevated early-life CORT exposure will result in long-term dampening of baseline and stress-induced [CORT] to promote resource conservation, if such exposure is an indicator of an unpredictable future resource conditions for this species (Haussmann et al., 2012; Love and Williams, 2008a). Alternatively, if elevated early CORT exposure is an indicator of high future predation rates, we predict exposed birds to display elevated baseline and stress-induced [CORT] to enhance fear and vigilance behaviors (Breuner, 2008; Haussmann et al., 2012). Previous work with these same house sparrows has shown that house sparrows exposed to elevated corticosterone at the nestling stage exhibit acute depression in growth followed by catch up growth at the juvenile stage (Grace et al., 2017a), poor antipredator behavior (Grace et al., 2017b), decreased male sexual ornamentation (Dupont et al., 2019), and increased mortality as adults (Grace et al., 2017a), but not whether this exposure affects the HPA axis stress response. Here, we specifically tested whether post-natal CORT exposure may affect circulating baseline and stress-induced CORT levels through adulthood. Because of the central role of CORT in mediating life-history trade-offs (Wingfield and Sapolsky 2003; Angelier and Wingfield 2013; Vitousek et al., 2018), exploring the developmental plasticity of the HPA axis will allow us to better understand how developmental conditions may orchestrate life-history strategies and life-history decisions in response to unpredictable events during various life-history stages.

2. Methods

All work was approved by the Centre National de la Recherche Scientifique and conforms to guidelines set forth by the French Ministry of Higher Education and Research and Ministry of Agriculture and Fisheries.

2.1. Study population and nestling manipulation

Nestling manipulation began at eight days post-hatching, and was conducted on free-living, wild house sparrows in the vicinity of the rural and agricultural town of Prissé la Charrière (46°09′12″N 0°28′59″W), Deux-Sèvres, France. All nests with more than one nestling in the study area were used and all nestlings were used in each nest (n = 131 nestlings). On day three post-hatching nestlings were given a plastic color band to facilitate individual identification, and on day 9 post-hatching nestlings were banded with a uniquely numbered permanent aluminum ring.

Corticosterone was delivered to nestlings non-invasively following the method of Breuner et al. (1998) and used successfully in subsequent studies (Breuner and Wingfield, 2000; Grace et al., 2017b,a; Lohmus et al., 2006; Saldanha et al., 2000). Meal worms were chilled at −20 °C to limit movement and were injected ventrally between exoskeletal segments into the central abdomen with 20 µl of 0.6 mg mL^{-1} CORT in dimethyl sulfoxide (DMSO), 0.9 mg mL^{-1} CORT in DMSO, or 20 µl of DMSO, alone. Mealworms that leaked were discarded. CORT-fed

nestlings received a CORT-injected worm on day 8 (0.6 mg mL^{-1}), day 9 (twice – morning and evening; 0.6 mg mL^{-1}), and day 11 post-hatching (0.9 mg mL^{-1}), while control nestlings received a DMSO-injected worm on the same schedule. This schedule discouraged habituation to treatment by limiting predictability. CORT concentrations were determined based on previous work with house sparrow nestlings (Loiseau et al., 2008) and Gambel's white-crowned sparrows (*Zonotrichia leucophrys*) (Breuner et al., 1998; Breuner and Wingfield, 2000), scaled to the average mass of house sparrow nestlings. This treatment increased circulating concentrations of CORT on average 8.6-fold within 40 min of worm ingestion for eight day old nestlings (CORT-fed: mean [CORT] ± SE = 76.74 ± 11.44 ng/mL; Control: 8.95 ± 1.45 ng/ mL) (Grace et al., 2017b), within the biologically relevant range for nestling house sparrows and that observed in response to natural stressors (Angelier et al., 2016).

Treatment began in the mid-late nestling period because the HPA axis may develop slowly in altricial species (Wada, 2008), but by eight days of age, a related species, the white-crowned sparrow is able to mount a strong HPA axis stress response (Wada et al., 2007). Half the nestlings in each nest were assigned to CORT-fed and control (DMSO-only) groups. CORT- and DMSO-injected worms were fed to nestlings with blunt-end forceps, at their nest box. Assignment was alternated between nestlings (e.g., CORT-fed first, control second, etc…) and assignment order was alternated between nests (e.g., CORT-fed first, control second; control first, CORT-fed second).

2.2. Captive housing

At and after twelve days post-hatching, nests were checked daily and nestlings that showed signs of flight were taken into captivity. Two or four nestlings (equal parts control and CORT-fed) were removed from each nest, resulting in birds from 23 nests in captivity. In three instances only three small fledglings were in the nest, thus, we brought all fledglings into captivity due to survival concerns (one of these died within one of week of captive housing). Fledglings were housed in wire bird cages (Vision S01, 45.5 × 35.5 × 51 cm) with all siblings (2–4 birds per cage) until birds reached basic plumage (i.e., adult stage), after which pairs consisting of one CORT-fed and one control bird were housed together. When possible these pairs were siblings, otherwise pairs were age- and sex-matched. Fledglings were hand-fed until they were capable of feeding on their own (mean ± s.e.m = 26.8 ± 4.8d, max = 41d, min = 18d). Following self-feeding, birds were supplied with mixed seeds *ad libitum*, vitamin and mineral soaked cat food, salt/mineral blocks, water (changed daily), and millet on the stalk. Grit was supplied three times per week and cages were equipped with perches of varying heights. Birds were kept on natural daylight schedules and caretakers were blind to treatment group.

2.3. Blood sampling and body measurements

We collected blood samples according to standardized stress-response protocol (Wingfield et al., 1992) at the pre-fledging (12 d post-hatching), juvenile (68–89 d post-hatching, juvenile plumage), and adult (173–185 d post-hatching, definitive basic plumage) stages (Table 1). Sampling was conducted between 0830 h and 1630 h, at least two hours after sunrise and two hours before sunset, and hour of sampling was included as a covariate in statistical analyses. We obtained an initial blood sample (~75 μl) immediately after initial disturbance (mean ± standard deviation = 2 min 18 s ± 44 s, max = 4 min) with 27-gauge needles and heparinized microcapillary tubes. Birds were then placed in cloth bags and a subsequent blood sample (~75 μl) was collected at approximately 32 min later (mean ± standard deviation = 31 min 59 s ± 2 min 47 s, max = 39 min 52 s) to monitor stress-induced [CORT]. There was no significant difference between baseline [CORT] from samples obtained at or prior to 3 min, compared to after 3 min ($t(28) = -0.49$, $p = 0.63$) or between stress-induced [CORT] from samples obtained prior to 35 min, compared to after 35 min ($t(1\ 2\ 7) = -0.20$, $p = 0.84$), thus all stress-induced [CORT] measures were used in analyses. All birds were weighed (electronic balance: ± 0.1 g), and tarsus (caliper: ± 0.1 mm) was measured. Tarsus length was chosen to represent body size because it is least prone to temporary damage that could alter measurements.

2.4. Corticosterone assays and molecular sexing

All laboratory analyses were performed at the Centre d'Etudes Biologiques de Chizé (CEBC). Immediately following collection, plasma was separated from the cellular fraction by centrifugation at 2000*g* for 7 min and plasma and red blood cells were preserved by freezing at −20 °C until analysis. Total plasma [CORT] was measured by radioimmunoassay as described in Lormée et al. (2003). Briefly, samples were extracted in ethyl ether, followed by radioimmunoassay using a commercial rabbit anti-serum against corticosterone-3-(O-carboxy-methyl) oxime bovine serum albumin conjugate (Biogenesis, UK). Cross-reaction was determined in a previous study to be 9% with 1-desoxycorticosterone and less than 0.1% with other plasma steroids (Lormée et al., 2003). Samples were run in duplicate. The minimum detectable [CORT] was 0.28 ng ml^{-1}, and the intra- and inter-assay coefficients of variation were 8.51% and 9.30% respectively.

Genomic DNA was extracted from frozen red blood cells using DNeasy Blood and Tissue Kits (Qiagen, Cat. No. 69504), a silica-based extraction method, according to the manufacturers protocol. Sex was assigned following the PCR protocol of Fridolfsson and Ellegren (1999) using two highly conserved genes (CHD) on the avian sex chromosomes. Sex assignment was confirmed by evaluation of sexual ornamentation in surviving adults. In all cases that could be confirmed by adult plumage, genetic sex matched plumage sex.

2.5. Statistical analyses

All statistical analyses were conducted in R (version 3.0.3) and were evaluated within a multimodel inference framework using the R packages 'lme4' (Linear Mixed-Effects Models using 'Eigen' and S4) and MuMIn (Multi-Model Inference). We ranked models using Akaike's Information Criterion corrected for small sample size (AICc) (Burnham et al., 2010), and evaluated models first by ΔAICc (the difference in AICc between the candidate model and the model with the lowest AICc), followed by examination of the beta coefficients and associated 95% confidence intervals (95% CI) (Anderson, 2008; Arnold, 2010). We report both marginal r-squared values (i.e., proportion of variance explained by fixed factors alone) and conditional r-squared values (i.e.,

Table 1
Demographic variables and mean [CORT] values for birds at the pre-fledging, juvenile, and adult life stages.

Life Stage	Number of Males	Number of Females	Nestlings per nest Mean ± SD	Baseline [CORT] Mean ± SD (ng ml^{-1})	Stress-induced [CORT] Mean ± SD (ng ml^{-1})
Pre-fledging	43	59	3.75 ± 1.00	9.51 ± 7.45	43.70 ± 27.78
Juvenile	29	41	3.23 ± 0.73	2.04 ± 2.26	14.63 ± 8.29
Adult	24	35	2.90 ± 0.74	1.86 ± 1.59	15.00 ± 9.00

the proportion of variance explained by both random and fixed factors) obtained by the delta method using the r.squaredGLMM function in R (Johnson, 2014; Nakagawa and Schielzeth, 2013).

We analyze baseline [CORT] (i.e., initial CORT concentration) and stress-induced [CORT] (i.e., CORT concentration 30 min after initial sample) within a repeated measures, generalized linear model framework (gamma family, log link), with nest of origin and bird ID as random effects. Preliminary analyses suggested important effects of hour of sampling, and two-way interactions between sample number (i.e., baseline or stress-induced sample) and sex, sample number and handling time, and three-way interactions between life stage (i.e., pre-fledgling, juvenile, adult), sample number, and current body condition, and between life stage, sample number, and mass at eight days post-hatching (when treatment began). Thus, these predictors and interactions were included in all models. We then compared models that included treatment, and interactions between treatment and the following variables: life stage, sample, sex, mass at eight days post-hatching (which could affect physiological concentration of CORT treatment), and current body condition because these had logical potential interactions with treatment (see Supplementary Information for all models). Our largest model had 35 degrees of freedom, with a sample size of 462, which was within general recommendations of 10 samples per degree of freedom. Body condition was the Scaled Mass Index (Peig and Green, 2009) of each bird, calculated from mass and tarsus length at the time of sampling, handling time was the number of seconds from disturbance until an initial blood sample was obtained for baseline [CORT], or the number of seconds from initial disturbance to final blood sample for stress-induced [CORT]. All continuous predictors were z-scored prior to analysis to prevent issues of scale.

3. Results

The top model by AICc selection (Table 2) included the fixed effects of treatment and hour of sampling, two-way interactions between sample number and sex, and sample number and handling time, and three-way interactions between sample number, life stage, and mass at 8 days post-hatching, and sample number, life stage, and current body condition (marginal $r^2 = 0.765$, conditional $r^2 = 0.798$; $N = 462$; Table 3). Early-life CORT treatment was associated with depressed [CORT] ($t = -3.10$, $p = 0.002$, $N = 462$, Table 3), with no interaction between treatment and sample number or treatment and life stage, indicating a consistently negative effect of treatment on baseline (Fig. 1) and stress-induced (Fig. 2) concentrations at all life stages. [CORT] decreased from the pre-fledging to the juvenile and adult stages, but that decrease was greater for baseline than stress-induced [CORT] (juvenile: $t = -12.78$, $p < 0.001$; adult: $t = -13.41$, $p < 0.001$; sample * juvenile: $t = 2.94$, $p = 0.003$; sample * adult: $t = 3.25$, $p = 0.001$, $N = 462$). Baseline [CORT] increased with mass at eight days post-hatching at the pre-fledging stage (Mass D8: $t = 3.15$, $p < 0.002$, $N = 462$, Fig. 3), but that effect disappeared by adulthood (Mass D8 * adult: $t = -2.64$, $p = 0.008$, $N = 462$, Fig. 3). Baseline [CORT] also decreased with current body condition at the pre-fledging stage ($t = -4.09$, $p < 0.001$, $N = 462$), an effect that also disappeared by adulthood (Body Condition * adult: $t = 3.28$, $p = 0.001$, $N = 462$, Fig. 4). Finally, baseline [CORT] increased with handling time (handling time: $t = 5.55$, $p < 0.001$, $N = 462$), and stress-induced [CORT] was higher in females than males (sample * sex: $t = 2.33$, $p = 0.02$, $N = 462$) and decreased with handling time (sample * handling time: $t = -4.86$, $p < 0.001$, $N = 462$).

Table 3
Beta coefficients and associated standard errors, t-values, and p-values for parameters in the top model predicting [CORT]. "Life Stage" indicates pre-fledging, juvenile, or adult life stages; "Sample" indicates baseline or stress-induced [CORT] sample; "Mass D8" is mass at eight days post-hatching (z-scored), when treatment began; "Handling Time" is the time in seconds after disturbance (z-scored); "Body Condition" is Scaled Mass Index (z-scored) calculated from mass and tarsus measurements; and "Hour" is the hour in which blood sampling occurred (z-scored). A: indicates an interaction term, and non-reference categories are in parenthesis for fixed factors.

Predictor	Beta	Standard Error	t-value	p-value
Treatment (CORT-fed)	−0.26	0.09	−3.10	0.002
Sample (stress-induced [CORT])	1.50	0.11	13.28	< 0.001
Life Stage				
Juvenile	−1.40	0.11	−12.78	< 0.001
Adult	−1.49	0.11	−13.41	< 0.001
Sex (Female)	−0.03	0.11	−0.27	0.790
Mass D8	0.23	0.07	3.15	0.002
Handling Time	0.26	0.05	5.55	< 0.001
Body Condition	−0.29	0.07	−4.09	< 0.001
Hour	−0.06	0.04	−1.54	0.123
Sample: Life Stage				
Sample: Juvenile	0.40	0.14	2.94	0.003
Sample: Adult	0.46	0.14	3.25	0.001
Sample: Mass D8	−0.18	0.09	−1.96	0.050
Sample: Sex	0.28	0.12	2.33	0.020
Sample: Handling Time	−0.31	0.06	−4.86	< 0.001
Sample: Body Condition	0.22	0.09	2.51	0.012
Life Stage: Mass D8				
Mass D8: Juvenile	−0.17	0.10	−1.67	0.094
Mass D8: Adult	−0.27	0.10	−2.64	0.008
Life Stage: Body Condition				
Body Condition: Juvenile	0.02	0.11	0.15	0.881
Body Condition: Adult	0.39	0.12	3.28	0.001
Sample: Mass D8: Life Stage				
Sample: Mass D8: Juvenile	0.10	0.13	0.84	0.403
Sample: Mass D8: Adult	0.26	0.13	2.03	0.042
Sample: Body Condition: Life Stage				
Sample: Body Condition: Juvenile	−0.11	0.14	−0.82	0.415
Sample: Body Condition: Adult	−0.49	0.15	−3.27	0.001

4. Discussion

In this study, we show that house sparrows exposed to early-life [CORT] elevation display both short- and long-term changes to the glucocorticoid stress response. Post-natal CORT treatment resulted in depressed baseline and stress-induced circulating CORT concentrations

Table 2
Model evaluation parameters for models predicting corticosterone concentration that are within Δ2 of the top model, and the first model to not include a treatment effect. Fixed model predictors are listed in the first column, followed by AIC model evaluation parameters. All models included the random effect of bird ID and nest of origin. A * indicates an interaction (and main effects), "Δ" indicates the difference between the AICc values of the top model and the model in question, and "df" is degrees of freedom. The smallest AICc value is 1066.32 and $N = 462$ for all models. "Life Stage" indicates pre-fledging, juvenile, or adult life stages; "Sample" indicates baseline or stress-induced [CORT] sample; "Mass D8" is mass at eight days post-hatching (z-scored), when treatment began; and "Hour" is the hour in which sampling occurred. Our top model, (i.e., the model with the lowest AICc) is highlighted in bold.

Model	df	Δ	Log Likelihood
Treatment + Sample * Life Stage * Mass D8 + Sample * Life Stage * Body Condition + Sample * Sex + Sample * Handling Time + Hour	**27**	**0.00**	**−1404.7**
Treatment * Life Stage + Sample * Life Stage * Mass D8 + Sample * Life Stage * Body Condition + Sample * Sex + Sample * Handling Time + Hour	29	0.52	−1402.6
Sample * Life Stage * Mass D8 + Sample * Life Stage * Body Condition + Sample * Sex + Sample * Handling Time + Hour	26	7.346	−1409.5

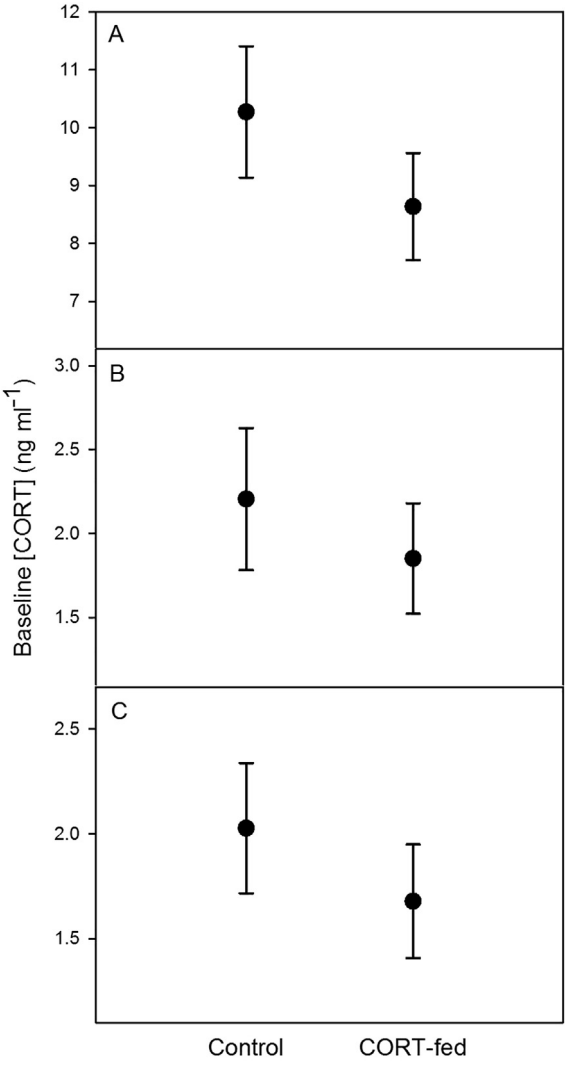

Fig. 1. Effect of treatment on baseline circulating [CORT] at the (A) pre-fledging (N = 103), (B) juvenile (N = 71), and (C) adult (N = 59) life stages. Note the different y-axis scale for each life stage. Dots are means, error bars are standard error.

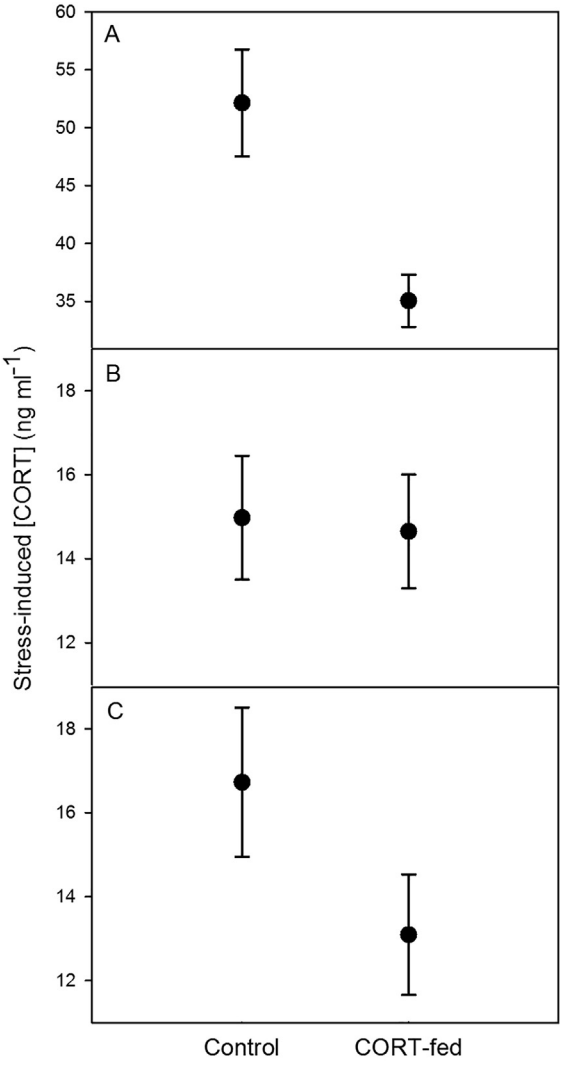

Fig. 2. Effect of treatment on stress-induced circulating [CORT] at the (A) pre-fledging (N = 103), (B) juvenile (N = 71), and (C) adult (N = 59) life stages. The y-axis indicates [CORT] after thirty minutes of handling stress. Note the different y-axis scale for pre-fledging birds. Dots are means, error bars are standard error. Although the effect of treatment appears to weaken at the juvenile stage, our model selection indicated a consistent negative effect of treatment across all life stages.

immediately following treatment and through adulthood. Post-natal body condition also positively affected baseline corticosterone concentration through adulthood, indicating effects of both glucocorticoid treatment and early-life nutritional state.

4.1. Effects of early-life mass and current body condition on the HPA axis

Nestling mass and current body condition and were found to have important effects on baseline circulating [CORT], especially at the pre-fledging stage. Nestling mass before treatment began positively predicted baseline [CORT] at the pre-fledging stage, independent of treatment, but that effect disappeared by adulthood. Consistent with these results, Lendvai et al. (2009) also found no effect of nestling mass on baseline or stress-induced [CORT] in adult house sparrows. This suggests that nestling mass does not have strong, long-term organizing effects on the HPA axis in this species.

Current body condition negatively predicted baseline [CORT] at the pre-fledging stage, consistent with some previous work in free-living species (e.g., Kitaysky et al., 1999; Wingfield et al., 1994), although others have found no relationship between body condition and baseline [CORT] (e.g., Breuner and Hahn, 2003; Lormée et al., 2003). The effect of body condition on [CORT] weakened at the juvenile stage, and by adulthood there was a weakly positive relationship between baseline [CORT] and body condition. This difference between the pre-fledging and adult stages could reflect life stage associated changes in the relationship between body condition and [CORT], and/or physiological changes in body composition associated with captivity. At the (wild) pre-fledging stage, body condition probably reflected nutritional conditions, which were standardized in captivity by the adult stage. Thus, body condition in adulthood may have reflected other aspects of health, and/or exercise or feeding frequency instead of nutritional state.

4.2. Effects of post-natal glucocorticoids on the HPA axis

Strong post-natal stressors are known to induce changes to the HPA axis in other captive, and some wild studies, but in contrast to our results, most studies find that the HPA axis becomes hypersensitized, resulting in elevated stress-induced CORT secretion (Grace and Anderson, 2018; Kalinichev et al., 2002; Pravosudov and Kitaysky, 2006; Schoech et al., 2011; Spencer et al., 2009), and typically no change in circulating baseline [CORT] (Grace and Anderson, 2018;

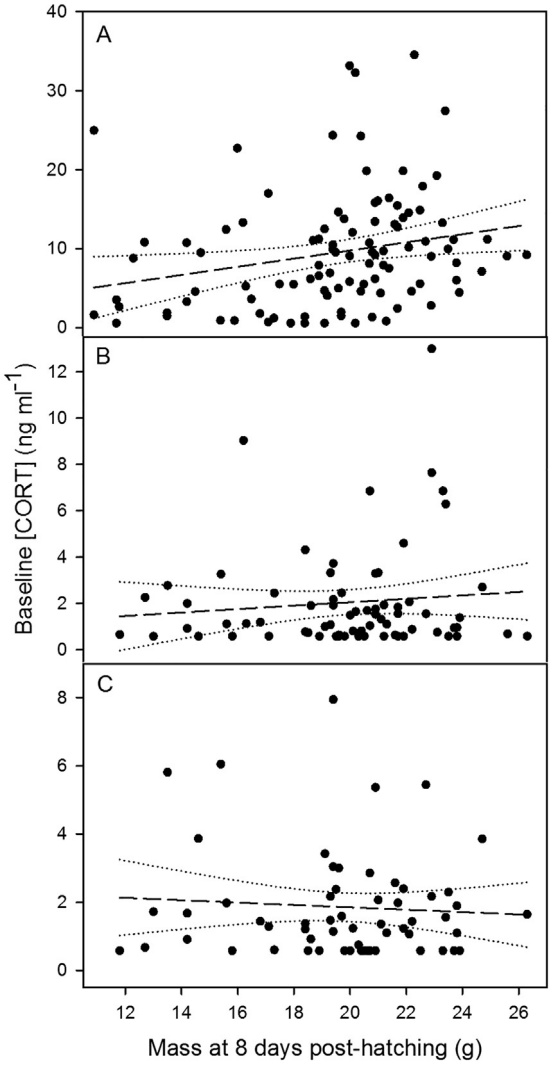

Fig. 3. Effect of mass at eight days post-hatching, before treatment began, on baseline [CORT] at the (A) pre-fledging (N = 103), (B) juvenile (N = 71), and (C) adult (N = 59) life stages. Dots represent data points for individual birds, long dashed lines are regression lines and dotted lines are confidence intervals. Nestling mass is negatively related to baseline [CORT] at the pre-fledging stage, and that effect weakens and disappears in later life stages.

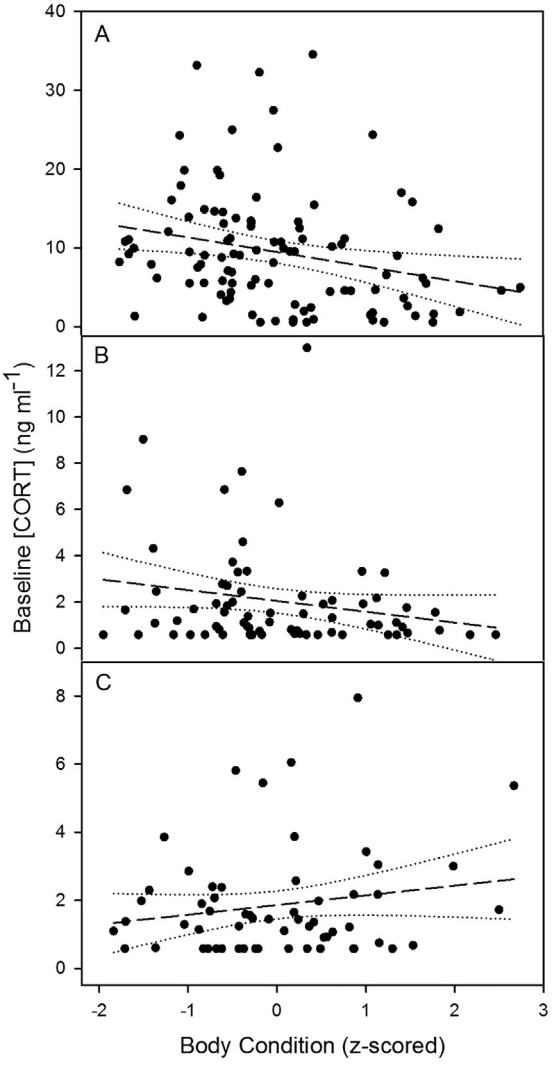

Fig. 4. Effect of current body condition (z-scored) on baseline [CORT] at the (A) pre-fledging (N = 103), (B) juvenile (N = 71), and (C) adult (N = 59) life stages. Dots represent data points for individual birds, long dashed lines are regression lines and dotted lines are confidence intervals. Body condition is z-scores of the Scaled Mass Index calculated using body mass and tarsus data at each life stage. Body condition has a negative relationship with baseline [CORT] at the pre-fledging stage, but that effect weakens, then becomes slightly positive by the adult stage.

Pravosudov and Kitaysky, 2006; Schoech et al., 2011; Spencer et al., 2009). However, this trend toward hypersensitivity following early-life stressor exposure is by no means universal. Domestic chickens (*Gallus gallus*), European starlings (*Sturnus vulgaris*), and some laboratory rodents display a decrease in HPA-axis sensitivity following chronic and/or early-life stressor experience, consistent with our own findings (Goerlich et al., 2012; Rich and Romero, 2005; Romero, 2004). These differences in the HPA-axis response to early-life stressor experience may be due to methodological or species-specific differences. Timing and intensity of stressor experience are known to alter short- and long-term HPA-axis responses both between and within species (Liu et al., 2000; Lyons et al., 2009; Marasco et al., 2012; Matthews, 2002; Schoech et al., 2011). For example, precocial Japanese quail (*Coturnix coturnix japonica*) exhibit higher HPA axis responses in adulthood following pre-natal corticosterone treatment, but no change following post-natal treatment (Marasco et al., 2012). Species-specific differences in life-history may also influence responses to stressors (Henriksen et al., 2011).

HPA-axis hyposensitivity following stressor experience could be due to (1) physiological exhaustion from stressor experience, (2) habituation to the stressor, or (3) downregulation of the HPA-axis stress response (Rich and Romero, 2005). Physiological exhaustion from stressor exposure is an unlikely explanation in our study because responses were measured across the lifespan; long-after stress treatment had ended. Birds were fed *ad libitum* and body condition quickly recovered once independent feeding was achieved post-treatment (Grace et al., 2017a). Regarding habituation, our treatment was designed to discourage habituation to stressor timing. Additionally, both control and CORT-fed birds were exposed to identical handling stress during and after treatment, providing equal opportunity for habituation in these two groups. However, glucocorticoids are known to enhance memory consolidation (Roozendaal, 2002), and early-life stressors can have long-term positive effects on associative learning (Brust et al., 2014; Goerlich et al., 2012; Kriengwatana et al., 2015). Habituation occurs more quickly when associative learning is high (Duerr and Quinn, 1982). Thus, CORT-fed birds may have habituated more quickly to human handling due to enhanced learning and memory of handling events compared to control birds. For this to explain our pre-fledgling

results, however, habituation would have had to occur very quickly. Finally, HPA-axis hyposensitivity could be due to downregulation of the HPA-axis stress response, a potentially adaptive organizational effect in response to post-natal stress exposure. The physiological/neurological mechanisms of reduced HPA activity in our study is unknown, but may include changes to glucocorticoid and mineralocorticoid receptors, or the serotonergic system (Banerjee et al., 2012; Matthews, 2002; Zimmer and Spencer, 2014).

4.3. HPA axis downregulation: an evolutionary perspective

HPA axis hyposensitivity in this study may indicate adaptive downregulation of the physiological stress response under the Match-Mismatch Hypothesis, if early-life GC exposure indicates an unpredictable or low quality future environment (Breuner, 2008; Gluckman and Hanson, 2004; Love and Williams, 2008a). Although no long-term effects of post-natal CORT on growth or body condition occur in this population (Grace et al., 2017a), post-natal CORT exposure does reduce nestling size and induce catch-up growth during the juvenile stage (Grace et al., 2017a). Reduced size and body condition at fledging is consistent with known acute GC effects on metabolism (Schmidt et al., 2012; Spencer and Verhulst, 2008; Verhulst et al., 2006). Circulating GCs typically increase in vertebrates in response to non-voluntary fasting (Landys et al., 2006) or to a drop in body temperature, as occurs when an incubating female is absent from the nest (Lynn and Kern, 2018). In house sparrows, specifically, stress-induced [CORT] is higher for fledglings who had low nestling body mass, suggesting a GC response to nutritional stress (Lendvai et al., 2009). Thus, our experimental increase in circulating [CORT] coupled with decreased nestling body condition and size would be consistent with indicators of unpredictable resources.

Downregulated GCs may be beneficial under poor quality or unpredictable environments for several reasons. First, desensitization of the HPA-axis response may be necessary to avoid the high energetic and other costs of frequently elevated circulating glucocorticoids in an unpredictable environment (Angelier and Wingfield, 2013; Goerlich et al., 2012; Rich and Romero, 2005; Sapolsky et al., 2000). Second, dampened baseline and stress-induced GCs can function to conserve glucose, thus depressed HPA activity may promote resource tracking and enhance survival in an environment with unpredictable resources (Breuner, 2008; Haussmann et al., 2012; Love and Williams, 2008a). The captive environment, and *ad libitum* food availability of our study unfortunately did not provide an opportunity to test this potential benefit to survival. However, the energy conservation benefits of downregulated GCs probably come at a cost to high energy behaviors enhanced by GCs, including vigilance and fear-related behaviors that may promote survival if predation risk is high (Breuner, 2008; Haussmann et al., 2012).

Previous work in this population has confirmed detrimental effects of post-natal CORT exposure on adult anti-predator behavior (Grace et al., 2017b), which may be mediated by long-term effects on circulating GCs. Fitness effects of post-natal CORT have also been identified in this population. Mortality risk is positively associated with the degree of compensatory juvenile growth (Grace et al., 2017a), which is a widespread consequence of poor neonatal nutrition (Metcalfe and Monaghan, 2001) and post-natal GC exposure (Grace et al., 2017a; Spencer et al., 2009), suggesting that GCs may be mediators of this trade-off between growth and longevity (Grace et al., 2017a; Metcalfe and Monaghan, 2003). Mortality risk may also be affected by long-term effects of downregulated GCs on the immune response. Baseline GCs permissively mediate immune responses within moments of exposure to a stressor, while stress-induced GCs play a critical role in restraining the immune and inflammatory responses and preventing pathological overshoot (reviewed in Sapolsky et al., 2000). Downregulated GCs may thus decrease survival if mortality risk is dominated by predation or infection, but increase survival if dominated by resource availability or quality (Haussmann et al., 2012).

GCs have a complicated relationship with reproductive success in other studies (Crespi et al., 2013; Sapolsky et al., 2000) that may reflect predominantly indirect effects on reproduction (Sapolsky et al., 2000). Baseline GCs are elevated during reproduction in oviparous species (Crespi et al., 2013), positively associated with brood value between bird species (Bókony et al., 2009), but can be positively (e.g., Chastel et al., 2005), negatively (e.g., Angelier et al., 2013), or not associated with reproductive success (Bonier et al., 2009). Stress-induced GCs have similarly variable relationships with reproductive success (Crespi et al., 2013), and are negatively related in some species (Crespi et al., 2013), and unrelated in others (e.g., Angelier et al., 2013). Previous work in this population of house sparrows suggests that post-natal CORT exposure may have negative effects on reproductive success for males by decreasing male sexual ornamentation (Dupont et al., 2019). Future studies are needed to determine if timing of breeding, pairing success, and numbers of offspring produced are affected by current or post-natal CORT exposure in this species.

5. Conclusions

In summary, we show that post-natal, developmental corticosterone exposure at stress-induced concentrations is associated with long-term depression of both baseline and stress-induced circulating [CORT], through adulthood in wild, captive house sparrows. These results are broadly consistent with the Match-Mismatch Hypothesis in that downregulated glucocorticoids may promote a phenotype of resource conservation (Breuner, 2008; Haussmann et al., 2012; Love and Williams, 2008a), which would enhance survival in the wild under unpredictable or variable resource conditions. The HPA axis stress response is well recognized for mediating life-history trade-offs during perturbations, by reallocating resources to immediate survival from other life-history components (Angelier et al., 2013; Crespi et al., 2013; Wingfield and Sapolsky, 2003). Thus, a downregulated HPA axis stress response would be expected to promote increased reproductive effort under unpredictable conditions, but would be detrimental to survival under conditions of high predation, for instance, in which a strong response is necessary for fight-or-flight success. Early-life programming of the HPA axis is one tool that vertebrates may use to maximize the fitness benefit from these trade-offs, when the early-life environment is predictive of the future mature environment.

CRediT authorship contribution statement

Jacquelyn K. Grace: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Charline Parenteau:** Methodology, Validation, Data curation, Supervision, Resources. **Frédéric Angelier:** Conceptualization, Methodology, Project administration, Funding acquisition, Resources, Supervision, Writing - review & editing.

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Appendix A. Supplementary data

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References

Adkins-Regan, E., Mansukhani, V., Seiwert, C., Thompson, R., 1994. Sexual differentiation of brain and behavior in the zebra finch: critical periods for effects of early estrogen treatment. J. Neurobiol. 25, 865–877. https://doi.org/10.1002/neu.480250710.

Anderson, D., 2008. Information theory and entropy. Model based inference in the life sciences: A primer on evidence. Springer, New York.

Angelier, F., Costantini, D., Blévin, P., Chastel, O., 2017. Do glucocorticoids mediate the link between environmental conditions and telomere dynamics in wild vertebrates? A review. Gen. Comp. Endocrinol. https://doi.org/10.1016/j.ygcen.2017.07.007.

Angelier, F., Meillère, A., Grace, J.K., Trouvé, C., Brischoux, F., 2016. No evidence for an effect of traffic noise on the development of the corticosterone stress response in an urban exploiter. Gen. Comp. Endocrinol. 232, 43–50. https://doi.org/10.1016/j.ygcen.2015.12.007.

Angelier, F., Wingfield, J.C., 2013. Importance of the glucocorticoid stress response in a changing world: theory, hypotheses and perspectives. Gen. Comp. Endocrinol. 190, 118–128. https://doi.org/10.1016/j.ygcen.2013.05.022.

Angelier, F., Wingfield, J.C., Trouvé, C., de Grissac, S., Chastel, O., 2013. Modulation of the prolactin and the corticosterone stress responses: do they tell the same story in a long-lived bird, the Cape petrel? Gen. Comp. Endocrinol. 182, 7–15. https://doi.org/10.1016/j.ygcen.2012.10.008.

Arnold, T., 2010. Uninformative parameters and model selection using Akaike's Information Criterion. J. Wildlife Manage. 74 (6), 1175–1178. https://doi.org/10.2193/2009-367.

Arnold, A.P., Breedlove, S.M., 1985. Organizational and activational effects of sex steroids on brain and behavior: a reanalysis. Horm. Behav. 19, 469–498. https://doi.org/10.1016/0018-506X(85)90042-X.

Banerjee, S.B., Arterbery, A.S., Fergus, D.J., Adkins-Regan, E., 2012. Deprivation of maternal care has long-lasting consequences for the hypothalamic-pituitary-adrenal axis of zebra finches. Proc. R. Soc. B Biol. Sci. 279, 759–766. https://doi.org/10.1098/rspb.2011.1265.

Boccia, M.L., Pedersen, C.A., 2001. Brief vs. long maternal separations in infancy: contrasting relationships with adult maternal behavior and lactation levels of aggression and anxiety. Psychoneuroendocrinology 26, 657–672.

Bókony, V., Lendvai, A.Z., Liker, A., Angelier, F., Wingfield, J.C., Chastel, O., 2009. Stress response and the value of reproduction: are birds prudent parents? Am. Nat. 173, 589–598. https://doi.org/10.1086/597610.

Bonier, F., Martin, P.R., Moore, I.T., Wingfield, J.C., 2009. Do baseline glucocorticoids predict fitness? Trends Ecol. Evol. 24, 634–642. https://doi.org/10.1016/j.tree.2009.04.013.

Breuner, C., 2008. Maternal stress, glucocorticoids, and the maternal/fetal match hypothesis. Horm. Behav. 54, 485–487. https://doi.org/10.1016/j.yhbeh.2008.05.013.

Breuner, C.W., Greenberg, A.L., Wingfield, J.C., 1998. Noninvasive corticosterone treatment rapidly increases activity in Gambel's white-crowned sparrows (Zonotrichia leucophrys gambelii). Gen. Comp. Endocrinol. 111, 386–394. https://doi.org/10.1006/gcen.1998.7128.

Breuner, C.W., Hahn, T.P., 2003. Integrating stress physiology, environmental change, and behavior in free-living sparrows. Horm. Behav. 43, 115–123. https://doi.org/10.1016/S0018-506X(02)00020-X.

Breuner, C.W., Wingfield, J.C., 2000. Rapid behavioral response to corticosterone varies with photoperiod and dose. Horm. Behav. 37, 23–30. https://doi.org/10.1006/hbeh.1999.1554.

Brust, V., Krüger, O., Naguib, M., Krause, E.T., 2014. Lifelong consequences of early nutritional conditions on learning performance in zebra finches (Taeniopygia guttata). Behav. Processes 103, 320–326. https://doi.org/10.1016/j.beproc.2014.01.019.

Burnham, K., Anderson, D., Huyvaert, K., 2010. AIC model selection and multimodel inference in behavioral ecology: some background, observations, and comparisons. Behav. Ecol. Sociobiol. 65, 23–35. https://doi.org/10.1007/s00265-010-1029-6.

Chastel, O., Lacroix, A., Weimerskirch, H., Gabrielsen, G.W., 2005. Modulation of prolactin but not corticosterone responses to stress in relation to parental effort in a long-lived bird. Horm. Behav. 47, 459–466. https://doi.org/10.1016/j.yhbeh.2004.10.009.

Cottrell, E.C., Seckl, J.R., 2009. Prenatal stress, glucocorticoids and the programming of adult disease. Front. Behav. Neurosci. 3, 1–9. https://doi.org/10.3389/neuro.08.019.2009.

Crespi, E.J., Williams, T.D., Jessop, T.S., Delehanty, B., 2013. Life history and the ecology of stress: how do glucocorticoid hormones influence life-history variation in animals? Funct. Ecol. 27, 93–106. https://doi.org/10.1111/1365-2435.12009.

Crino, O.L., Breuner, C.W., 2015. Developmental stress: evidence for positive phenotypic and fitness effects in birds. J. Ornithol. 156, 389–398. https://doi.org/10.1007/s10336-015-1236-z.

Crino, O.L., Driscoll, S.C., Breuner, C.W., 2014a. Corticosterone exposure during development has sustained but not lifelong effects on body size and total and free corticosterone responses in the zebra finch. Gen. Comp. Endocrinol. 196, 123–129. https://doi.org/10.1016/j.ygcen.2013.10.006.

Crino, Ondi L., Prather, C.T., Driscoll, S.C., Good, J.M., Breuner, C.W., 2014b. Developmental stress increases reproductive success in male zebra finches. Proc. R. 281, 20141266. https://doi.org/10.1098/rspb.2014.1266.

Drummond, H., Ancona, S., 2015. Observational field studies reveal wild birds responding to early-life stresses with resilience, plasticity, and intergenerational effects. Auk 132, 563–576. https://doi.org/10.1642/AUK-14-244.1.

Duerr, J.S., Quinn, W.G., 1982. Three Drosophila mutations that block associative learning also affect habituation and sensitization. Proc. Natl. Acad. Sci. U.S.A. 79, 3646–3650.

Dupont, S.M., Grace, J.K., Brischoux, F., Angelier, F., 2019. Post-natal corticosterone exposure affects ornaments in adult male house sparrows (Passer domesticus). Gen. Comp. Endocrinol. 276, 45–51.

Durand, M., Sarrieau, A., Aguerre, S., Mormède, P., Chaouloff, F., 1998. Differential effects of neonatal handling on anxiety, corticosterone response to stress, and hippocampal glucocorticoid and serotonin (5-HT)2A receptors in Lewis rats. Psychoneuroendocrinology 23, 323–335.

Fridolfsson, A.-K., Ellegren, H., 1999. A simple and universal method for molecular sexing of non-ratite birds. J. Avian Biol. 30, 116–121.

Gluckman, P., Hanson, M., Beedle, A., 2007. Early life events and their consequences for later disease: a life history and evolutionary perspective. Am. J. Hum. Biol. 19, 1–19. https://doi.org/10.1002/ajhb.

Gluckman, P.D., Hanson, M.A., 2004. Living with the past: evolution, development, and patterns of disease. Science (80-.) 305, 1733–1736.

Goerlich, V.C., Nätt, D., Elfwing, M., Macdonald, B., Jensen, P., 2012. Transgenerational effects of early experience on behavioral, hormonal and gene expression responses to acute stress in the precocial chicken. Horm. Behav. 61, 711–718. https://doi.org/10.1016/j.yhbeh.2012.03.006.

Grace, J.K., Anderson, D.J., 2018. Early-life maltreatment predicts adult stress response in a long-lived wild bird. Biol. Lett. 14, 20170679. https://doi.org/10.1098/rsbl.2017.0679.

Grace, J.K., Froud, L., Meillère, A., Angelier, F., 2017a. House sparrows mitigate growth effects of post-natal glucocorticoid exposure at the expense of longevity. Gen. Comp. Endocrinol. 253, 1–12. https://doi.org/10.1016/j.ygcen.2017.08.011.

Grace, J.K., Martin-Gousset, L., Angelier, F., 2017b. Delayed effect of early-life corticosterone treatment on adult anti-predator behavior in a common passerine. Physiol. Behav. 177, 82–90. https://doi.org/10.1016/j.physbeh.2017.04.018.

Haussmann, M.F., Longenecker, A.S., Marchetto, N.M., Juliano, S.A., Bowden, R.M., 2012. Embryonic exposure to corticosterone modifies the juvenile stress response, oxidative stress and telomere length. Proc. Biol. Sci. 279, 1447–1456. https://doi.org/10.1098/rspb.2011.1913.

Henriksen, R., Rettenbacher, S., Groothuis, T.G.G., 2011. Prenatal stress in birds: pathways, effects, function and perspectives. Neurosci. Biobehav. Rev. 35, 1484–1501. https://doi.org/10.1016/j.neubiorev.2011.04.010.

Johnson, P.C.D., 2014. Extension of Nakagawa & Schielzeth's R2GLMM to random slopes models. Methods Ecol. Evol. 5, 944–946. https://doi.org/10.1111/2041-210X.12225.

Kalinichev, M., Easterling, K.W., Plotsky, P.M., Holtzman, S.G., 2002. Long-lasting changes in stress-induced corticosterone response and anxiety-like behaviors as a consequence of neonatal maternal separation in Long-Evans rats. Pharmacol. Biochem. Behav. 73, 131–140.

Kitaysky, A.S., Kitaiskaia, E.V., Piatt, J.F., Wingfield, J.C., 2003. Benefits and costs of increased levels of corticosterone in seabird chicks. Horm. Behav. 43, 140–149. https://doi.org/10.1016/S0018-506X(02)00030-2.

Kitaysky, A.S., Piatt, J.F., Wingfield, J.C., Romano, M., 1999. The adrenocortical stress-response of Black-legged Kittiwake chicks in relation to dietary restrictions. J. Comp. Physiol. B Biochem. Syst. Environ. Physiol. 169, 303–310. https://doi.org/10.1007/s003600050225.

Kriengwatana, B., MacDougall-Shackleton, S.A., Farrell, T.M., Garcia, L., Aitken, S.D.T., 2015. Early-life nutritional stress affects associative learning and spatial memory but not performance on a novel object test. Behaviour 152, 195–218. https://doi.org/10.1163/1568539X-00003239.

Landys, M.M., Ramenofsky, M., Wingfield, J.C., 2006. Actions of glucocorticoids at a seasonal baseline as compared to stress-related levels in the regulation of periodic life processes. Gen. Comp. Endocrinol. 148, 132–149. https://doi.org/10.1016/j.ygcen.2006.02.013.

Lendvai, Á.Z., Loiseau, C., Sorci, G., Chastel, O., 2009. Early developmental conditions affect stress response in juvenile but not in adult house sparrows (*Passer domesticus*). Gen. Comp. Endocrinol. 160, 30–35. https://doi.org/10.1016/j.ygcen.2008.10.004.

Lindström, J., 1999. Early development and fitness in birds and mammals. Trends Ecol. Evol. 14, 343–348. https://doi.org/10.1016/S0169-5347(99)01639-0.

Liu, D., Caldji, C., Sharma, S., Plotsky, P.M., Meaney, M.J., 2000. Influence of neonatal rearing conditions on stress-induced adrenocorticotropin responses and norepinepherine release in the hypothalamic paraventricular nucleus. J. Neuroendocrinol. 12, 5–12.

Lohmus, M., Sundstrom, L.F., Moore, F.R., 2006. Non-invasive corticosterone treatment changes foraging intensity in red-eyed vireos *Vireo olivaceus*. J. Avian Biol. 37, 523–526.

Loiseau, C., Sorci, G., Dano, S., Chastel, O., 2008. Effects of experimental increase of corticosterone levels on begging behavior, immunity and parental provisioning rate in house sparrows. Gen. Comp. Endocrinol. 155, 101–108. https://doi.org/10.1016/j.ygcen.2007.03.004.

Lormée, H., Jouventin, P., Trouve, C., Chastel, O., 2003. Sex-specific patterns in baseline corticosterone and body condition changes in breeding Red-footed Boobies, Sula sula. Ibis (Lond. 1859). 145, 212–219. doi: 10.1046/j.1474-919X.2003.00106.x.

Love, Oliver P., Williams, T.D., 2008a. Plasticity in the adrenocortical response of a free-living vertebrate: the role of pre- and post-natal developmental stress. Horm. Behav. 54, 496–505. https://doi.org/10.1016/j.yhbeh.2008.01.006.

Love, Oliver P., Williams, T.D., 2008b. The adaptive value of stress-induced phenotypes:

effects of maternally derived corticosterone on sex-biased investment, cost of reproduction, and maternal fitness. Am. Nat. 172, E135–E149. https://doi.org/10.1086/590959.
Lucassen, P.J., Naninck, E.F.G., van Goudoever, J.B., Fitzsimons, C., Joels, M., Korosi, A., 2013. Perinatal programming of adult hippocampal structure and function; emerging roles of stress, nutrition and epigenetics. Trends Neurosci. 36, 621–631. https://doi.org/10.1016/j.tins.2013.08.002.
Lynn, S.E., Kern, M.D., 2018. Interactions of body temperature and nutritional status on hypothalamo-pituitary-adrenal axis activity in pre-thermoregulatory eastern bluebird chicks (*Sialia sialis*). Gen. Comp. Endocrinol. 267, 82–89. https://doi.org/10.1016/j.ygcen.2018.06.003.
Lyons, D.M., Parker, K.J., Katz, M., Schatzberg, A.F., 2009. Developmental cascades linking stress inoculation, arousal regulation, and resilience. Front. Behav. Neurosci. 3, 32. https://doi.org/10.3389/neuro.08.032.2009.
Marasco, V., Robinson, J., Herzyk, P., Spencer, K., 2012. Pre- and post-natal stress in context: effects on the stress physiology in a precocial bird. J. Exp. Biol. 215, 3955–3964. https://doi.org/10.1242/jeb.071423.
Matthews, S.G., 2002. Early programming of the hypothalamo-pituitary-adrenal axis. Trends Endocrinol. Metab. 13, 373–380.
McEwen, B.S., Wingfield, J.C., 2003. The concept of allostasis in biology and biomedicine. Horm. Behav. 43, 2–15. https://doi.org/10.1016/S0018-506X(02)00024-7.
Metcalfe, N.B., Monaghan, P., 2003. Growth versus lifespan: perspectives from evolutionary ecology. Exp. Gerontol. 38, 935–940. https://doi.org/10.1016/S0531-5565(03)00159-1.
Metcalfe, N.B., Monaghan, P., 2001. Compensation for a bad start: Grow now, pay later? Trends Ecol. Evol. 16, 254–260. https://doi.org/10.1016/S0169-5347(01)02124-3.
Monaghan, P., 2008. Early growth conditions, phenotypic development and environmental change. Philos. Trans. R. Soc. London B Biol. Sci. 363, 1635–1645. https://doi.org/10.1098/rstb.2007.0011.
Nakagawa, S., Schielzeth, H., 2013. A general and simple method for obtaining R2 from generalized linear mixed-effects models. Methods Ecol. Evol. 4, 133–142. https://doi.org/10.1111/j.2041-210x.2012.00261.x.
Nederhof, E., Schmidt, M.V., 2012. Mismatch or cumulative stress: toward an integrated hypothesis of programming effects. Physiol. Behav. 106, 691–700. https://doi.org/10.1016/j.physbeh.2011.12.008.
Pakkala, J.J., Norris, D.R., Sedinger, J.S., Newman, A.E.M., 2016. Experimental effects of early-life corticosterone on the hypothalamic – pituitary – adrenal axis and pre-migratory behaviour in a wild songbird. Funct. Ecol. 30, 1149–1160. https://doi.org/10.1111/1365-2435.12603.
Peig, J., Green, A.J., 2009. New perspectives for estimating body condition from mass/length data: the scaled mass index as an alternative method. Oikos 118, 1883–1891. https://doi.org/10.1111/j.1600-0706.2009.17643.x.
Pravosudov, V.V., Kitaysky, A.S., 2006. Effects of nutritional restrictions during post-hatching development on adrenocortical function in western scrub-jays (*Aphelocoma californica*). Gen. Comp. Endocrinol. 145, 25–31. https://doi.org/10.1016/j.ygcen.2005.06.011.
Rich, E.L., Romero, L.M., 2005. Exposure to chronic stress downregulates corticosterone responses to acute stressors. Am. J. Physiol. Regul. Integr. Comp. Physiol. 288, 1628–1636. https://doi.org/10.1152/ajpregu.00484.2004.
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.
Roozendaal, B., 2002. Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval. Neurobiol. Learn. Mem. 78, 578–595. https://doi.org/10.1006/nlme.2002.4080.
Saldanha, C.J., Schlinger, B.A., Clayton, N.S., 2000. Rapid effects of corticosterone on cache recovery in mountain chickadees (Parus gambeli). Horm. Behav. 37, 109–115. https://doi.org/10.1006/hbeh.2000.1571.
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.
Schmidt, K.L., Macdougall-Shackleton, E., Macdougall-Shackleton, S., 2012. Developmental stress has sex-specific effects on nestling growth and adult metabolic rates but no effect on adult body size or body composition in song sparrows. J. Exp. Biol. 215, 3207–3217. https://doi.org/10.1242/jeb.068965.
Schmidt, K.L., MacDougall-Shackleton, E.A., Soma, K.K., MacDougall-Shackleton, S.A., 2014. Developmental programming of the HPA and HPG axes by early-life stress in male and female song sparrows. Gen. Comp. Endocrinol. 196, 72–80. https://doi.org/10.1016/j.ygcen.2013.11.014.
Schoech, S.J., Rensel, M.A., Heiss, R.S., 2011. Short- and long-term effects of developmental corticosterone exposure on avian physiology, behavioral phenotype, cognition, and fitness: a review. Curr. Zool. 57, 514–530. https://doi.org/10.1093/czoolo/57.4.514.
Seckl, J.R., 2004. Prenatal glucocorticoids and long-term programming. Eur. J. Endocrinol. 151, U49–U62.
Slotten, H.A., Kalinichev, M., Hagan, J.J., Marsden, C.A., Fone, K.C.F., 2006. Long-lasting changes in behavioural and neuroendocrine indices in the rat following neonatal maternal separation: gender-dependent effects. Brain Res. 1097, 123–132. https://doi.org/10.1016/j.brainres.2006.04.066.
Spencer, K.a., Verhulst, S., 2007. Delayed behavioral effects of postnatal exposure to corticosterone in the zebra finch (*Taeniopygia guttata*). Horm. Behav. 51, 273–280. https://doi.org/10.1016/j.yhbeh.2006.11.001.
Spencer, Karen A., Evans, N.P., Monaghan, P., 2009. Postnatal stress in birds: a novel model of glucocorticoid programming of the hypothalamic-pituitary-adrenal axis. Endocrinology 150, 1931–1934. https://doi.org/10.1210/en.2008-1471.
Spencer, K.A., Verhulst, S., 2008. Post-natal exposure to corticosterone affects standard metabolic rate in the zebra finch (*Taeniopygia guttata*). Gen. Comp. Endocrinol. 159, 250–256. https://doi.org/10.1016/j.ygcen.2008.09.007.
Verhulst, S., Holveck, M.-J., Riebel, K., 2006. Long-term effects of manipulated natal brood size on metabolic rate in zebra finches. Biol. Lett. 2, 478–480. https://doi.org/10.1098/rsbl.2006.0496.
Vitousek, M., Taff, C., Hallinger, K., Zimmer, C., Winkler, D., 2018. Hormones and fitness: evidence for trade-offs in glucocorticoid regulation across contexts. Front. Ecol. Evol. 6 (April), 1–14. https://doi.org/10.3389/fevo.2018.00042. 42.
Wada, H., 2008. Glucocorticoids: mediators of vertebrate ontogenetic transitions. Gen. Comp. Endocrinol. 156, 441–453. https://doi.org/10.1016/j.ygcen.2008.02.004.
Wada, H., Hahn, T.P., Breuner, C.W., 2007. Development of stress reactivity in white-crowned sparrow nestlings: total corticosterone response increases with age, while free corticosterone response remains low. Gen. Comp. Endocrinol. 150, 405–413. https://doi.org/10.1016/j.ygcen.2006.10.002.
Welberg, L.A.M., Seckl, J.R., 2001. Prenatal stress, glucocorticoids and the programming of the brain. J. Neuroendocrinol. 13, 113–128.
Wingfield, J.C., Maney, D.L., Breuner, C.W., Jacobs, J.D., Lynn, S., Ramenofsky, M., Richardson, R.D., 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". Integr. Comp. Biol. 38, 191–206. https://doi.org/10.1093/icb/38.1.191.
Wingfield, J.C., Sapolsky, R.M., 2003. Reproduction and resistance to stress: when and how. J. Neuroendocrinol. 15, 711–724.
Wingfield, J.C., Suydam, R., Hunt, K., 1994. The adrenocortical responses to stress in snow buntings (Plectrophenax nivalis and Lapland longspurs (Calcarius lapponicus) at Barrow, Alaska. Comp. Biochem. Physiol. – Part C Comp. Pharmacol. Toxicol. 108C, 299–306. https://doi.org/10.1016/0742-8413(94)00030-E.
Wingfield, J.C., Vleck, C.M., Moore, M.C., 1992. Seasonal-changes of the adrenocortical-response to stress in birds of the Sonoran desert. J. Exp. Zool. 264, 419–428. https://doi.org/10.1002/jez.1402640407.
Zimmer, C., Boogert, N.J., Spencer, K.A., 2013. Developmental programming: cumulative effects of increased pre-hatching corticosterone levels and post-hatching unpredictable food availability on physiology and behaviour in adulthood. Horm. Behav. 64, 494–500. https://doi.org/10.1016/j.yhbeh.2013.07.002.
Zimmer, C., Spencer, K.A., 2014. Modifications of glucocorticoid receptors mRNA expression in the hypothalamic-pituitary-adrenal axis in response to early-life stress in female Japanese quail. J. Neuroendocrinol. 26, 853–860. https://doi.org/10.1111/jne.12228.
https://github.com/lme4/lme4/, 1.1-21.
http://cran.rproject.org/package=MuMIn, 1.43.15.