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REVIEW

Detrimental or beneficial? Untangling the literature on developmental stress studies in birds

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ABSTRACT

Developing animals display a tremendous ability to change the course of their developmental path in response to the environment they experience, a concept referred to as developmental plasticity. This change in behavior, physiology or cellular processes is primarily thought to allow animals to better accommodate themselves to the surrounding environment. However, existing data on developmental stress and whether it brings about beneficial or detrimental outcomes show conflicting results. There are several well-referred hypotheses related to developmental stress in the current literature, such as the environmental matching, silver spoon and thrifty phenotype hypotheses. These hypotheses speculate that the early-life environment defines the capacity of the physiological functions and behavioral tendencies and that this change is permanent and impacts the fitness of the individual. These hypotheses also postulate there is a trade-off among organ systems and physiological functions when resources are insufficient. Published data on avian taxa show that some effects of developmental nutritional and thermal stressors are long lasting, such as the effects on body mass and birdsong. Although hypotheses on developmental stress are based on fitness components, data on reproduction and survival are scarce, making it difficult to determine which hypothesis these data support. Furthermore, most physiological and performance measures are collected only once; thus, the physiological mechanisms remain undertested. Here, we offer potential avenues of research to identify reasons behind the contrasting results in developmental stress research and possible ways to determine whether developmental programming due to stressors is beneficial or detrimental, including quantifying reproduction and survival in multiple environments, measuring temporal changes in physiological variables and testing for stress resistance later in life.

KEY WORDS: Nutritional stress, Heat stress, Cold stress, Development, Birds

Introduction

The environmental conditions that developing organisms experience have robust and long-lasting effects on their phenotypes. Body size, physiological functions and behavioral tendencies are shaped by these developmental conditions and can influence survival and reproductive success of the individual (Lindström, 1999). At the same time, the observed consequences of early life conditions vary considerably. Not surprisingly, there is a debate among stress biologists whether suboptimal developmental conditions allow animals to flourish in a comparable environment or, instead, reduce reproductive potential and/or shorten lifespan.

Several hypotheses have aimed at explaining the context dependency in the outcome of developmental stressors (see Glossary). The environmental matching hypothesis postulates that the early-life environment molds individuals to perform well in the forecasted adult environment (Monaghan, 2008). Thus, when environmental conditions are stable across the lifespan, individuals' fitness is maximized regardless of the quality of the environment. In contrast, the silver spoon hypothesis predicts that animals which grow up in a good environment always outperform animals that grow up in a poor environment, regardless of the adult environment (Grafen, 1988; Monaghan, 2008). This occurs when a poor early-life environment constrains proper development and maturation of organ systems and physiological functions (Nord and Giroud, 2020). The combination of the environmental matching and silver spoon hypotheses is the thrifty phenotype hypothesis. It aims to explain the epidemiological data showing that low birth and body weight in 1 year old humans are associated with high rates of cardiovascular disease and diabetes (Hales and Barker, 1992, 2001). According to this hypothesis, the fitness of an individual who grows up in a poor environment always falls behind that of an individual from a good environment and is expected to decrease as the adult environment improves (Monaghan, 2008). All three hypotheses predict that individuals from a good rearing environment have higher fitness in a good adult environment compared with ones from a poor rearing environment, but the degree of differences differs. More importantly, predictions among the three hypotheses vary in a poor adult environment, highlighting the importance of collecting data under suboptimal environmental conditions to determine which hypothesis is supported.

In addition to the above-mentioned hypotheses, the trade-off theory has been well studied in the context of developmental stressors. It predicts that when resources are scarce, development and maturation of one or more organ system(s) is prioritized over others. This prioritization results in proper development of particular organs, often predicted to be the ones that are more essential for survival, while hindering the development of other organs. The developmental stress hypothesis is based on the trade-off theory (Spencer and MacDougall-Shackleton, 2011). It posits that birdsong is a good indicator of male quality because its development is costly and there is a trade-off in allocating resources to various organ systems when the developmental environment is stressful (Nowicki et al., 1998, 2002; Spencer and MacDougall-Shackleton, 2011). The time young songbirds learn to feed on their own coincides with the time that brain regions responsible for learning and producing song, i.e. song nuclei, develop. When food availability is low, prioritizing resource allocation towards somatic growth over song nuclei can result in low song complexity.

To test these hypotheses, a great number of studies have applied a stressor during development that mimics stressors experienced in

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Glossary

Catch-up growth
This occurs when birds, after the end of treatment, grow at a rapid rate to 'catch up' to the body mass and size of their control counterparts or surpass them as they reach adulthood.

Developmental asymmetry
When the size of an appendage on one side is significantly different from the size of the same appendage on the other side of the organism

Heat shock proteins (HSPs)
A family of molecular chaperones which aid in repairing damage, such as DNA damage and protein misfolding, caused by cellular stressors (Dubrez et al., 2020; Feder and Hofmann, 1999).

Hormesis
A phenomenon whereby a low-level stressor triggers a favorable response whereas a high-level stressor leads to a harmful response (Agathokleous et al., 2019; Calabrese, 2013).

HVC
One of the song nuclei in birds; formerly called the high vocal center.

Latent effect
When an effect of a stressor appears at some time after the initial exposure

Song complexity
The number of syllables and songs in a repertoire, or other components of birdsong that, with more or fewer of these components, changes the quality of the song.

Song learning
The acquisition of species-specific song during development in birds.

Stressor
A stimulus that has the potential to cause molecular, cellular, organ or tissue damage in an animal (Wada, 2019).

Stress resilience
An animal's ability to restore performance after a temporary decline.

Stress resistance
An animal's ability to elicit behavioral, physiological or cellular responses to avoid persistent damage such that the animals' performance is unaffected.

Stress tolerance
An animal's ability to maintain performance even when stressors result in some level of persistent damage. When the level of accumulated damage passes a tolerance threshold, performance starts to decline (Wada, 2019).

Thermoneutral zone
A range of ambient temperatures at which a homeotherm can maintain its core body temperature without increasing metabolic rate.

Thyroid hormones
One of the major regulators of metabolism; involved in body temperature regulation (Mullur et al., 2014). The thyroid gland predominantly produces thyroxine (T4), which is then converted to a more active form, triiodothyronine (T3), at the target tissue.

Transgenerational effect
Effects in organisms that can alter the phenotype of their descendants in subsequent, unexposed generations (i.e. F3).

the wild, such as suboptimal temperature, food deprivation, high population density, environmental toxins and hypoxia. In this Review, we focus on two common stressors in avian taxa: nutritional and thermal stress. We chose the avian taxa because there exists a wide range of studies that have tested the above-mentioned hypotheses using these stressors. These studies include ones on agricultural species, laboratory model species and wild birds. Nutritional stress has gathered attention in the field partly because of the developmental stress hypothesis (Nowicki et al., 1998). As a result, the majority of the studies examining the effects of nutritional stress have been carried out in songbirds, where song quality, song nuclei or corticosterone (one of the stress hormones) is measured. In contrast, thermal stress studies are done primarily in poultry, where researchers are interested in how to promote thermal tolerance in broilers and laying hens through hot summers to maximize survival and yield. Keeping these differences in mind, we categorized studies by nutritional and thermal stress. Despite the wealth of studies, it has been challenging to determine when developmental stressors bring beneficial or costly outcomes later in life, to identify which hypothesis the existing data support the most and to pinpoint the cause of varying results. In this Review, we will identify assumptions in existing hypotheses, gaps in knowledge and additional measures needed to decipher whether developmental stressors are beneficial or detrimental and offer recommendations for areas of future research.

Effects of developmental stressors on stress tolerance and fitness measures

In this section, we briefly summarize common findings in nutritional and thermal manipulation studies, highlighting whether stress tolerance (see Glossary), reproductive output and survival have been measured in these studies.

Nutritional manipulation

Nutritional stress involves any significant change in nutrition that is below optimal, such as caloric restriction and varying macronutrient availability. There are several different ways nutritional stress is administered, making it difficult to draw general conclusions about the outcomes of nutritional stress during development. Here, we categorize the studies by four ways nutrition was manipulated. The first is through food restriction, where the quality of food remains the same, but the amount of food provided to stressed individuals is less than in the control group. Secondly, food removal studies remove food at a random time of day for a specified length of time, whereas the control group has unlimited access to the same quality of food. The focus of this type of study is to investigate how unpredictability, rather than quantity of food, changes how individuals develop. Thirdly, increased foraging time studies, often used with birds, provide food mixed with inedible items that require individuals to search harder for their food compared with controls (Lemon, 1993). Lastly, in food quality studies, animals can eat *ad libitum*, but the macronutrient availability in the diet varies between treatment groups.

Generally, food restriction negatively impacts song learning (see Glossary) and complexity (see Glossary), growth and hormone levels. Male birds that have experienced food restriction as nestlings copy tutor songs less accurately compared with controls (Nowicki et al., 2002; Schmidt et al., 2013) (Table S1). One mechanism that links food restriction to song quality is a reduction in song nuclei volume, although the duration of the stressor influences its effect (Nowicki et al., 2002; MacDonald et al., 2006). As birds sing to attract a mate, food restriction can be detrimental if the change in birdsong lowers reproductive success. However, the effect of food restriction during development on fitness components is largely undertested. Additionally, birds under food restriction experience greater developmental asymmetry (see Glossary) and slower growth compared with unstressed birds (Pravosudov and Kitaysky, 2006; Kempster et al., 2007). Food-restricted females also had lower circulating levels of estradiol than controls, indicating a potential detriment to reproduction (Schmidt et al., 2014). Further studies are necessary to determine whether this change in estradiol decreases reproductive success.

Food removal generally hinders song complexity and learning, motivation to sing, growth rate and stress hormones. Birds subjected to this regime had smaller song repertoires, sang less and took

longer to start singing (Buchanan et al., 2003; Spencer et al., 2004). One mechanism behind the observed changes in birdsong could be corticosterone, as stressed birds had higher corticosterone titers compared with controls. Food removal studies show mixed results for body mass; whereas some showed that stressed birds weighed less than control birds (Chin et al., 2013; Ericsson et al., 2016), others showed the opposite effect (Buchanan et al., 2003; Farrell et al., 2012; Goerlich et al., 2012; Farrell et al., 2015a). Unpredictability in food availability can cause some animals to consume more food when it is available, increasing overall food intake and body mass, which could explain this disparity. Further research is needed to determine whether these changes in growth rate impact the attractiveness, reproductive effort or success of affected individuals.

Similar to food restriction and food removal, food mixed with inedible items (to increase foraging time in the lab) tends to hinder song learning and complexity, mate choice behavior and growth rate. Birds from nests with a higher foraging effort had lower song learning accuracy, lower song complexity and lower motivation to sing than controls (Spencer et al., 2003, 2005; Brumm et al., 2009; Bell et al., 2018). In another study, there was no effect on song-learning accuracy, but stressed males had lower song complexity than controls (Zann and Cash, 2008). Other studies observed that birds from nests with increased foraging effort had a smaller HVC (see Glossary) volume and decreased ability to remember novel songs compared with controls (Buchanan et al., 2004; Bell et al., 2018), suggesting that lower song complexity in the stressed birds may be due to an alteration in the song nuclei. These detriments to song components have been shown to affect mate choice, where females prefer non-stressed males (Spencer et al., 2005). Furthermore, stressed females have been shown to be less active in mate choice trials (Woodgate et al., 2010). This effect could decrease reproductive success, although this link has not been measured thoroughly in foraging studies. Additionally, birds forced to forage for longer weighed less during development, but they experienced catch-up growth (see Glossary) (Metcalfe and Monaghan, 2001; Spencer et al., 2003; Brumm et al., 2009; Woodgate et al., 2010; Kriengwatana et al., 2013). The decreased growth rate during treatment could be due to corticosterone, as stressed birds elevate baseline corticosterone levels in the developmental period (Kriengwatana et al., 2014). However, the exact mechanism for catch-up growth and whether it has long-term consequences on behavioral tendencies or survival remains untested.

In contrast to other types of nutritional stress studies, food quality has mixed effects on mate choice and behavior, and detrimental effects on growth rate. For mate choice, one study found that females preferred males that received high-quality food when given a choice (Naguib and Nemitz, 2007), whereas other studies did not observe this effect (Honarmand et al., 2015, 2017). Another study found that males given low-quality food spent more time with females that received the same treatment than with those that received high-quality food (Noguera et al., 2017). These results may be due to differences in sexually selected traits. In the zebra finch, females preferred males with redder beaks (Simons and Verhulst, 2011), and food quality was positively correlated with redness of the bills (Noguera, 2017). For birdsong, another sexually selected trait, birds given lower quality food had higher song rates compared with birds given high-quality food (Honarmand et al., 2015). This result is in contrast to those from other nutritional stress studies, which observed reduced song measures in the stress groups (Nowicki et al., 2002; Buchanan et al., 2003; Spencer et al., 2003, 2004, 2005; Brumm et al., 2009; Schmidt et al., 2013; Bell et al., 2018). There are also mixed results on reproductive efforts. Whereas one study found that low-quality diet negatively impacted clutch size, another study found no effect of diet quality on clutch size and other measures of reproductive success (Honarmand et al., 2017; Noguera et al., 2017). Because of the mixed results on reproductive variables, additional data are necessary to determine how diet quality affects reproduction. Regarding other fitness effects, quality of food in birds does not appear to influence survival or survival of the offspring of stressed individuals (Honarmand et al., 2010; Krause and Naguib, 2014; Honarmand et al., 2017). For behavior, birds on a low-quality diet as juveniles were more aggressive, less responsive to handling stress, less neophobic and learned some tasks better in adulthood than individuals on a high-quality diet (Brust et al., 2014; Noguera et al., 2015). Although there are also mixed results on exploratory behavior (Krause et al., 2009; Krause and Naguib, 2011, 2014, 2015), fast learning and possessing bold characteristics can give competitive advantages to stressed birds, especially when food resources are limited.

In summary, developmental nutritional stress often decreases song quality and induces catch-up growth. However, it is difficult to generalize a pattern because of mixed results. This is in part due to variation in the stressor application (i.e. methodology and timing), duration and severity of the stressor and timing of sample collection. Importantly, there may be a missed opportunity to measure variables that are more directly related to fitness, particularly under a nutritionally stressful environment as adults. What differs the most between the environmental matching, silver spoon and thrifty phenotype hypotheses is the fitness outcome in the poor adult environment, which is currently lacking in nutritional stress studies.

Thermal manipulation

For the purpose of this paper, we focus on studies that directly manipulate the temperature that the developing animals experience, rather than ones that manipulate environmental conditions of the parents or nest box temperatures (see Andreasson et al., 2020, for a review of the latter topic). This is because manipulation of the parental environment or nest box temperatures addresses a different set of questions, particularly trade-offs between current reproduction and survival for the parents. Avian embryos have a narrow range of temperatures that they can tolerate compared with other oviparous species (Webb, 1987; Du and Shine, 2015), and both temperature and stability of temperature are important for their development (Olson et al., 2008, 2006; Rubin et al., 2021; Stier et al., 2020). Here, we refer to conditioning as exposing young to a mild heat or cold treatment (during incubation or after hatching). Moreover, we define a challenge as exposing juveniles or adults to more severe heat or cold to assess stress tolerance of the conditioned and control individuals in order to distinguish between stressors that are applied at different stages of life for a distinct purpose. In contrast to nutritional stress studies, thermal manipulation studies are found mostly in agricultural species, which are precocial species and artificially selected. Although heat-conditioning studies in chickens and wild birds have been reviewed elsewhere (see Loyau et al., 2015, and Nord and Giroud, 2020, for details), we emphasize here the fitness effects of both heat and cold conditioning and possible mechanisms behind them.

Common findings for short-term conditioning

Heat conditioning of domesticated chickens for 4 or 24 h within 1 week of hatching improves survival during a heat challenge at market age, an age at which chickens are moved to a processing

plant (Loyau et al., 2015). This is likely attributed to the fact that heat-conditioned chickens can maintain lower body temperature during an acute heat challenge compared with non-conditioned individuals (Ncho et al., 2021). Similarly, when chicken embryos are exposed to heat stress for a short period of time, they tend to be better equipped to handle increased ambient temperatures as juveniles and adults (Nord and Giroud, 2020). For instance, embryonic heat conditioning (at 39.5°C) for 2–3 h when the hypothalamic–pituitary–thyroid (HPT) axis of chickens is developing [around embryonic day (E) 10 and 13 (McNabb, 1989; Thommes, 1987)] improves heat tolerance at 34 or 42 days post-hatch (dph) (Piestun et al., 2011, 2008; but also see Collin et al., 2007). This heat tolerance is evident by higher survival rates at otherwise lethal or near-lethal temperatures or the ability to avoid hyperthermia during such a heat challenge compared with controls (Piestun et al., 2008).

Interestingly, an 18 h per day heat treatment as embryos not only improves heat tolerance but also improves cold tolerance, as shown by improved survival during a 5 day cold challenge at 32–37 dph (Saleh et al., 2020). These results indicate that embryonic exposure to suboptimal temperature may alter cellular or physiological pathways that are common protective mechanisms against thermal stressors. Furthermore, chicks briefly (30 or 60 min) exposed to 15°C twice during the last part of the incubation period (E18 and 19) recovered their body temperature faster after a cold challenge at 3 and 14 dph, and had a lower mortality during a cold challenge and reduced incidence of ascites (fluid accumulation in the abdominal cavity) compared with the controls (Shinder et al., 2009, 2011). In general, these results from short-term conditioning studies in poultry support the environmental matching hypothesis (Nord and Giroud, 2020).

Thyroid hormones (see Glossary), heat shock proteins (HSPs; see Glossary) and antioxidants have been proposed to facilitate this acquisition of thermal tolerance. In a study with broiler chickens, triiodothyronine (T3) levels were lower in embryos and chicks exposed to high incubation temperatures, which was accompanied by lower body temperatures and heat production around hatching compared with controls (Tona et al., 2008; Yahav and Hurwitz, 1996; Yahav and McMurtry, 2001; Yahav and Plavnik, 1999; Yahav et al., 2004b; reviewed in Ruuskanen et al., 2021; but also see Yahav et al., 2004a). Although others report that all animals had reduced T3 levels during a heat challenge, the reduction was greater in conditioned animals compared with non-conditioned animals (Moraes et al., 2003; Piestun et al., 2011, 2008; Tona et al., 2008; Yahav and McMurtry, 2001). Furthermore, laying hens heat conditioned for 6 h per day during the latter half of the incubation period had decreased thyroxin (T4) levels after a heat challenge and increased T4 levels after a cold challenge (Kamanli et al., 2015). Although metabolic rate was not measured in this study, these results indicate that these animals can potentially match metabolic rate to the ambient temperature better than non-conditioned animals through an alteration of the HPT axis.

In vitro studies indicate that a prior exposure to mild heat enhances cell survival at otherwise lethal temperatures via increased expression of HSPs (Moseley, 1997; Moseley et al., 1994; Rattan and Ali, 2007; Samali et al., 1999). Conversely, results related to the role of HSPs in heat tolerance *in vivo* are mixed (Shehata et al., 2020). Heat-conditioned animals tend to have higher levels of HSPs compared with controls. For instance, heat-conditioned and heat-conditioned/food-restricted chickens had elevated HSP70 protein levels in the brain during a 2 week heat challenge, whereas non-conditioned animals did not (Liew et al., 2003). In broilers, the duration of heat conditioning likely determines the level of HSPs, as heat conditioning (60 min per day) that lasted 1 week increased HSP90 and HSP70 protein levels, whereas 2 week heat conditioning did not (Wang and Edens, 1998). In another study with broilers, heat-conditioned chickens had reduced levels of HSPs (Yahav et al., 1997a,b). Thus, more studies are needed to examine the role of HSPs in acquired heat tolerance.

Thermal stress can elevate levels of reactive oxygen species (ROS) and oxidative damage in a cell if excess amounts of ROS are not neutralized (Mujahid et al., 2007, 2005; reviewed in Abdel-Moneim, 2021). Because antioxidants can neutralize free radicals, they are thought to enable thermal resistance. Cold temperature can cause cellular and tissue damage in broiler chickens (Julian, 2000; Wei et al., 2018; Zhang et al., 2011); thus, upregulation of antioxidants and other repair mechanisms can help minimize cold-associated damage. In fact, the conditioned hens that had experienced mild cold as embryos elevated superoxide dismutase antioxidant activity significantly more after a cold challenge compared with non-conditioned hens (Kamanli et al., 2015). Another study in broilers found that mild cold conditioning (e.g. 3–7°C lower than controls) during the juvenile period enhanced antioxidant enzyme activities (Li et al., 2017). However, severe thermal stress can hinder protective mechanisms, as an exposure to severe cold (e.g. a sudden 13°C drop) decreases antioxidant activities (broilers: Wei et al., 2018). It is possible that, when exposed to mild levels of cold stress, antioxidants are upregulated to minimize cold-associated oxidative damage to DNA, proteins and lipids. In contrast, when exposed to severe cold stress, the antioxidant system may be overwhelmed by free radicals or antioxidant levels may decrease as a result of damage to the antioxidant production pathway, leading to reduced levels of antioxidants available to neutralize free radicals (Zhang et al., 2009, 2018).

Common findings for long-term conditioning

In contrast to short-term exposure to high incubation temperature, constantly high incubation temperature resulted in lower hatching success in chickens (Piestun et al., 2008) and zebra finches (Wada et al., 2015). Constant, high incubation temperature also led to a higher rate of malformations in chickens, often showing multiple malformations in one embryo (Noiva et al., 2014). Long-term heat conditioning also does not appear to provide thermotolerance in chickens in the way short-term heat conditioning does. For instance, 3 week heat conditioning of broilers right after hatching did not improve heat tolerance between 36 and 50 dph (Liew et al., 2003). Some of these results support the silver spoon hypothesis (Nord and Giroud, 2020) given that heat exposure during development has a negative consequence on hatching success, whereas other results do not support one particular hypothesis.

Three studies thus far have examined the effects of a 28 day juvenile heat-conditioning treatment on oxidative damage, survival and reproductive performance in zebra finches (Costantini et al., 2012, 2014; Hoffman et al., 2018). When birds were exposed to high heat (42°C) 3 h per day for 3 consecutive days as adults, the birds that underwent mild heat conditioning as juveniles (at 38°C) had lower plasma oxidative damage compared with non-conditioned birds and ones that were conditioned to high heat (42°C) as juveniles (Costantini et al., 2012). These results indicate that the severity of a stressor determines the ability to combat a future stressor. Furthermore, survival after adult treatment depended on a match between juvenile and adult treatment, where non-conditioned individuals that were exposed to high heat as adults and heat-conditioned individuals that were not exposed to heat again as

adults had lower survival than those with 'matching' juvenile and adult treatments (Costantini et al., 2014). These results suggest that there is a cost to priming cellular and physiological functions in response to increased temperatures, which is precipitated when developmental and adult environments do not match. Interestingly, juvenile conditioning with mild heat (at 38°C) and exposure to high heat (42°C) as adults for 3 days independently improved percentage fertility in a clutch, indicating heat exposure enhances reproductive performance in zebra finches at those time points (Hoffman et al., 2018). In contrast to long-term heat conditioning in chickens, these results support the environmental matching hypothesis when the conditioning temperature is within the species' thermoneutral zone (see Glossary).

Similar to long-term heat conditioning studies, long-term cold conditioning generally has a negative impact on offspring performance. Constant low incubation temperature resulted in high protein usage (Hepp et al., 2006), high metabolic rates (DuRant et al., 2011; Olson et al., 2006) and reduced thermoregulatory ability (Black and Burggren, 2004) during the incubation period in wood ducks, zebra finches and chickens. The effect of long-term cold conditioning lasted at least for the first 1–3 weeks of life, as shown by low body condition (i.e. lower body mass for the size) in the cold conditioned animals at or after hatching (DuRant et al., 2010), high metabolic rates (Nord and Nilsson, 2011; Wada et al., 2015) and high energy expenditure during a cold challenge (DuRant et al., 2012). Furthermore, zebra finches and American robins exposed to constantly low incubation temperature as embryos had a lower post-hatching survival (Berntsen and Bech, 2016; Ospina et al., 2018; Wada et al., 2015; but also see Nord and Nilsson, 2016), indicating a long-term effect of cold conditioning on fitness components.

When are suboptimal developmental conditions beneficial or detrimental?

Whether a developmental stressor enhances or reduces fitness-related measures (therefore bringing beneficial or detrimental outcomes) depends on the duration, severity and timing of the stressor, as well as the timing of the performance measurement and the stability of the environment throughout the experiment for each experimental group. In general, a short exposure to suboptimal temperatures as an embryo and soon after hatching enhances thermotolerance later in life, thus supporting the environmental matching hypothesis (Nord and Giroud, 2020). In contrast, constant or long-term thermal stress during incubation decreases hatching success and increases the incidence of the malformation and post-hatch survival (Noiva et al., 2014; Piestun et al., 2008; Wada et al., 2015). These data in part support the silver spoon hypothesis (Nord and Giroud, 2020) and indicate that severe or prolonged thermal stress likely hinders proper development. This biphasic response fits the framework of hormesis (see Glossary), where short exposure may induce a maximum response of the inverted U-shaped (concave) curve whereas long-term exposure pushes the response from adaptive to maladaptive (Calabrese, 2013). The concept is particularly interesting for developmental stressors because the hormetic dose–response curve can quantify a limit of plasticity and where an adaptive response turns into a maladaptive response (Agathokleous et al., 2019). This hormetic response may be due to alterations in the HPT axis and other physiological changes triggered by the developmental conditions, which are likely to have a cost when the animal's environment changes. Likewise, food restriction is known to negatively impact birdsong, but the severity of damage to the song nucleus depends on the duration of the nutritional stressor and the sensitivity of specific brain regions to the physiological response induced by the stressor. In previous studies, HVC growth was stunted first, and the telencephalon and robust nucleus of the arcopallium also experienced decreased growth if the duration of the stressor increased (Nowicki et al., 2002; MacDonald et al., 2006). At the same time, a change in birdsong has rarely been examined together with attractiveness and reproductive effort; thus, it is premature to conclude whether shorter and simpler songs due to food restriction are ultimately detrimental.

The overall outcome of the developmental stressor depends on the balance between benefits and costs (Loeschcke and Hoffmann, 2002). When the stressor is too harsh and inflicts persistent damage to the individual, the costs of the developmental conditions may mask the beneficial effects (Wilson and Franklin, 2002). For instance, higher than optimal incubation temperature can lower hatching success (costs) (Piestun et al., 2008). But among those that hatch, high incubation temperature often improves thermotolerance in adulthood (benefits) (Piestun et al., 2008). Therefore, the same suboptimal condition is costly for hatching success but possibly bears benefits for thermotolerance. This example highlights scenarios where the conditions that enhance immediate survival may be different from those that improve stress tolerance later in life or long-term survival. In the case of zebra finches, a higher than optimal incubation temperature lowered hatching success, whereas a lower than optimal incubation temperature lowered post-hatch survival (Wada et al., 2015). Here, both suboptimally high and low incubation temperatures had the cost of lower survival, but at different life stages. In both cases, developmental stressors may weed out less tolerant individuals; thus, surviving animals may do equally well as or better than non-stressed individuals. Ultimately, to determine whether developmental stressors are beneficial or detrimental to the animal, studies must also test survival and/or reproductive success to evaluate whether the benefits outweigh the costs.

Existing hypotheses in context: assumptions and supporting evidence

Across the above-mentioned hypotheses, there are common assumptions and presumed mechanisms. One assumption is that the developmental environment has a permanent effect on physiological and cellular functions, such as endocrine and cellular stress responses. The silver spoon and thrifty phenotype hypotheses describe long-lasting effects of the developmental environment on the fitness of the individual (Monaghan, 2008). In the environmental matching hypothesis, fitness depends on whether early- and late-life environments match or not. All three hypotheses postulate a permanent change in physiological and cellular function as the root of such effects on fitness. But does the evidence point to a permanent change in physiological functions due to developmental stressors? Or do physiological and cellular functions remain plastic throughout one's life, despite being exposed to a developmental stressor?

Another assumption is that there is a trade-off among physiological systems, meaning the body prioritizes certain organ systems at the expense of others. The cost of this trade-off may manifest immediately or later in life. The trade-off theory is a proposed mechanism for impaired fitness under a poor early-life environment. Does evidence from the literature support the idea that organisms in a poor environment preferentially allocate resources to a particular organ system? Or is resource allocation reduced equally across organ systems, but various organs have different sensitivity to low resource availability? In this section, we

explore evidence in avian studies that supports or opposes the assumptions of a permanent change in physiological functions and trade-offs.

Assumption 1: physiological and cellular functions change permanently when exposed to a developmental stressor

In Tables 1 and 2, we have categorized studies and variable types such as hormone levels and metabolic rates into the types of effect that have been observed. The most concrete support for a permanent change in physiological and cellular function would come from studies that measured those variables repeatedly and saw a consistent decline or elevation after an exposure to a developmental stressor. Effects can also manifest later in life (a latent effect; see Glossary) or in the next generation (a transgenerational effect; see Glossary). These latent and transgenerational effects, if documented repeatedly, would also support the idea that an exposure to developmental stressors permanently changes physiological functions. In contrast, effects that diminish over time oppose the assumption that there is a permanent change in physiological or cellular functions due to developmental stressors. To distinguish between no effect and a latent effect or between a permanent effect and a diminishing effect, one must measure animals multiple times across their lifespan. Likewise, effects observed a long time after the treatment ceased, but only measured once, require further studies with repeated measures to confirm whether the change is persistent. It is also possible that effects can be detected only after the animal was challenged with a stressor later in life; and these effects are interesting for two reasons. Firstly, if the change occurs in conjunction with fitness-related measures, then the results would indicate a change in stress resistance (see Glossary). Secondly, they emphasize the importance of testing stress resistance and going beyond collecting samples only in a benign adult environment, because we may otherwise miss the effects of developmental stressors. Here, we focus on long-term modifications in levels of hormones, HSPs, antioxidants and metabolic rates as potential mechanisms of observed changes in birdsong, morphology and growth due to developmental stressors.

One of the main mechanisms proposed for reduced song learning or growth rate in response to restricted food availability is plasma corticosterone. Song learning starts soon after fledging and goes into early adulthood, spanning weeks for close-ended learners (Brainard and Doupe, 2002). If plasma corticosterone is the culprit for impaired song learning, we should observe a sustained elevation (or suppression if corticosterone is necessary for song learning) during one or more phases of song learning. In respect to growth rate, it is possible that reduced growth rate during the treatment is due to elevated baseline or stress-induced corticosterone, which may return to control-comparable levels after the treatment ceases, permitting catch-up growth. Generally, developmental nutritional stress does not alter baseline corticosterone levels (Schmidt et al., 2012; Zimmer et al., 2013; Ericsson et al., 2016), whereas stress-induced corticosterone levels show mixed results (Table 1). Although some studies documented an increase in stress-induced corticosterone due to nutritional stress (Buchanan et al., 2003; Pravosudov and Kitaysky, 2006; Ericsson et al., 2016), others showed no effect (Goerlich et al., 2012; Zimmer et al., 2013; Schmidt et al., 2014; Ericsson et al., 2016). Nutritional stress also does not typically influence metabolic rate (Krause et al., 2009; Schmidt et al., 2012; Chin et al., 2013; Kriengwatana et al., 2013; but also see Criscuolo et al., 2008). An artificial elevation of corticosterone impedes song learning (Spencer et al., 2003), yet nutritional stress studies that observed effects on birdsong did not consistently detect a change in corticosterone. These results do not strongly support the idea that a permanent change in corticosterone occurs in stress-exposed animals, or that elevated corticosterone during the critical period of development accompanies a change in birdsong or growth rate.

When considering corticosterone as one of the candidates for mediating the effects of developmental stress on growth and metabolic rate in thermal conditioning studies, some studies saw a long-term effect of developmental thermal manipulation on plasma corticosterone levels (DuRant et al., 2010; Moraes et al., 2003; Rubin et al., 2021; Tona et al., 2008), whereas others saw diminishing effects or no effects (DuRant et al., 2010; Wada et al., 2015) (Table 2). It is worth noting that, with the exception of a zebra finch study that documented an increase in corticosterone at the same time as an increase in metabolic rate (Wada et al., 2015), changes in corticosterone do not seem to coincide with changes in growth rate or metabolic rate. It is commonly thought that a high metabolic rate leads to high growth when food is abundant whereas a low metabolic rate leads to high growth when food is scarce (Auer et al., 2015; Killen et al., 2011; Derting, 1989). In a study with wood ducks, embryos incubated at the lowest temperature had the highest energy expenditure during incubation (DuRant et al., 2011) and the lowest growth rate for the first 9 days post-hatching (DuRant et al., 2010). In contrast, a study with zebra finches showed a brief elevation in metabolic rate in female fledglings from the lowest incubation temperature group, even though their growth rate during the fledging period or beyond was comparable to that of the controls (Wada et al., 2015). Thus, it is unclear whether developmental thermal stress causes a permanent change in metabolic rate or corticosterone levels, which could in turn mediate a treatment effect on growth rate.

Given its role in temperature regulation, a permanent change in thyroid hormone production or thyroid hormone metabolism via deiodination would support the idea that developmental thermal stress enhances thermoregulatory capacity via alteration of the HPT axis. Poultry studies show that alterations in the HPT axis and body temperature accompanied by thermal conditioning can last for 4–6 weeks (Moraes et al., 2003; Piestun et al., 2011), in some cases up to 30 weeks (Kamanli et al., 2015), mitigating hyperthermia and hypothermia during a thermal challenge. At the same time, the effect of thermal manipulation on thyroid hormone levels can diminish over time (Yahav and Hurwitz, 1996; Yahav et al., 1997b) or only emerge after a heat challenge (Moraes et al., 2003; Piestun et al., 2008; Tona et al., 2008) (Table 2). Further studies are needed to confirm whether a long-term change in the HPT axis, hormone metabolism and hormone receptor abundance correlate with acquired heat or cold tolerance.

In general, it is difficult to determine whether developmental stressors alter physiological and cellular functions permanently. The main reason for this is that developmental stress studies do not typically measure physiological and cellular functions across time. Therefore, the results of these studies can only be categorized as possible long-term effects or no effect. This is especially true for nutritional stress studies. More nutritional stress studies should sample multiple physiological and fitness-related variables repeatedly across time to determine whether changes in stress responses persist in the organism. An exception to this recommendation would be song variables. Close-ended learners have crystallized (fixed) songs; thus, measuring song characteristics multiple times may not be very informative. Open-ended learners continue to learn song throughout their lives (Brainard and Doupe,

Table 1. Overview of effects of developmental nutritional manipulation on physiological and cellular functions and organ mass in avian studies

	No effect	Diminishing effect	Long-term effect	Transgenerational
CORT	Baseline in treated individuals and their offspring, 30 min stress induced in treated individuals and their offspring (Ericsson et al., 2016); baseline (Schmidt et al., 2012); baseline, 10 and 30 min stress induced (Zimmer et al., 2013); stress-induced CORT, CORT response to DEX and ACTH (Schmidt et al., 2014); 10 and 30 min stress induced in female offspring of treated individuals (Goerlich et al., 2012).	↑ Baseline (Pravosudov and Kitaysky, 2006)	↑ Baseline (Honarmand et al., 2010); ↑10 min stress induced in 8 week stress group compared with all other groups, offspring of 8 week stress group compared with offspring of 2 week stress group (Ericsson et al., 2016); ↑20 and 50 min stress induced (Pravosudov and Kitaysky, 2006); ↑stress-induced titer (Buchanan et al., 2003)	↓ 10 and 30 min stress induced in male offspring of treated individuals (Goerlich et al., 2012).
Androgens	Androgen in females, peak androgen in males, integrated androgen in males (Farrell et al., 2015a); testosterone (Schmidt et al., 2014; Buchanan et al., 2003); testosterone in parents, in yolk testosterone on collection days 1 and 3 (Goerlich et al., 2012).		↓ Baseline androgens in males (Farrell et al., 2015a)	↑Yolk testosterone on collection day 2 (Goerlich et al., 2012).
Estradiol	Yolk estradiol on collection day 3 (Goerlich et al., 2012).		↓ Average estradiol (Schmidt et al., 2014)	↓ Yolk estradiol on collection day 1, ↑yolk estradiol on collection day 2 (Goerlich et al., 2012).
Metabolic rate	PMR, metabolic scope, SMR in males (Schmidt et al., 2012); RMR (Krause et al., 2009); BMR (Kriengwatana et al., 2013); oxygen consumption (Chin et al., 2013).		↑ SMR in females (Schmidt et al., 2012).	
Organ mass	Kidney, heart (Kriengwatana et al., 2013); pectoralis dry mass, supracoracoideus dry mass, pectoralis water content, supracoracoideous water content (Chin et al., 2013).		↑ In HL and LL female liver (Kriengwatana et al., 2013).	
Organ volume	Testes (Farrell et al., 2015a)			
TAC	(Noguera, 2017)			
Enzymatic antioxidant defense	On day of reproductive pairing, between diet groups in reduced broods (Noguera, 2017).		↑ Decline in GPx activity over time in fluctuating diet group with enlarged broods (Noguera, 2017)	
Oxidative DNA damage	(Noguera, 2017)			
Telomere length	(Noguera, 2017)			

Diminishing effect: changes due to a developmental stressor that diminish over time. Long-term effect: changes that were observed long after the treatment was halted (although the variable in questions was measured only once). Transgenerational: effects observed in the subsequent generation. Up and down arrows indicate an increase or a decrease relative to the controls. Gray boxes indicate effects that cannot be measured using current methods. No latent effects were observed using developmental nutritional stress. Empty cells indicate that this effect was not assessed.
CORT, corticosterone; LH, low then high food; HL, high then low food; LL, low food throughout experiment; HH, high food throughout experiment (all either by quality or amount of food, depending on the study, as defined by the study); PMR, peak metabolic rate; SMR, standard metabolic rate; RMR, resting metabolic rate; BMR, basal metabolic rate; GPx, glutathione peroxidase; TAC, total nonenzymatic antioxidant capacity.

2002); thus, a change in song duration, rate or complexity in adulthood may not reflect the animals' developmental environment. Previous studies also observed tissue specificity for some variables. For instance, effects of thermal manipulation on antioxidant levels and oxidative damage are heavily tissue specific. Similarly, changes in hormone metabolism and receptor abundance can change the efficacy of the hormones. As tissue antioxidants, oxidative damage and receptor levels are often terminal measures, there is a logistical hurdle for sampling repeatedly unless the animal is large enough to allow multiple tissue sampling.

Assumption 2: resources are preferentially allocated to particular organs

It is possible that, when exposed to a stressor, resource allocation is favored towards certain organs such as the brain or heart. Previous studies have shown that the brain is relatively buffered from nutritional and water deprivation, whereas the spleen, gonads and adipose tissues are not (Glazier, 2009). Referred to as brain-sparing, severe nutritional deprivation during mammalian fetal development increases blood delivery to the brain, while restricting blood flow to peripheral tissues via vascular remodeling (Cohen et al., 2015). It is

Table 2. Overview of effect of developmental thermal manipulation on physiological and cellular functions and organ mass in avian studies

	No effect	Latent effect	Diminishing effect	Long-term effect	Only after stress challenge
CORT	Baseline CORT [Moraes et al., 2003; Tona et al., 2008; Wada et al., 2015 (heat and cold); Rubin et al., 2021 (cold)]; adrenocortical response [Wada et al., 2015 (heat and cold; males only)]; response to ACTH [Wada et al., 2015 (heat and cold)]; response to Dex [Wada et al., 2015 (heat and cold)].		↑ Baseline CORT [DuRant et al., 2010 (high incubation temperature only)]; ↑adrenocortical response [DuRant et al., 2010 (high incubation temp only), Wada et al., 2015 (cold, females only)].	↑ Baseline CORT [DuRant et al., 2010 (low incubation temp only];↑adrenocortical response [DuRant et al., 2010 (low incubation temperature only)]; no↓in adrenocortical response (habituation) with age [Rubin et al., 2021 (cold)].	↓ CORT [Piestun et al., 2008; Yahav et al., 2004b (mild heat at late phase only)]; ↑CORT response (Tona et al., 2008).
Thyroid hormone	T4 (Moraes et al., 2003); T3 [Kamanli et al., 2015 (cold and heat)].	↑ T4 [Kamanli et al., 2015 (heat only)].	↓ T3 (Yahav and Hurwitz, 1996; Yahav et al., 1997a,b) (appeared again after heat stress).	↓ T3, ↓T4 (Piestun et al., 2011).	↓ T3 (Moraes et al., 2003; Piestun et al., 2008; Tona et al., 2008);↓T4 (Piestun et al., 2008); ↑T4 [Kamanli et al., 2015 (cold)].
HSP	(Liew et al., 2003)			↓ HSP70 after heat stress (Yahav et al., 1997a,b).	
Antioxidant and oxidative damage	GPx [Costantini et al., 2012; Kamanli et al., 2015 (heat and cold)]; non-enzymatic antioxidant capacity (Costantini et al., 2012); malondialdehyde [Kamanli et al., 2015 (heat and cold)].	↑ SOD [Kamanli et al., 2015 (heat and cold)].	↑ Plasma oxidative damage (high heat; Costantini et al., 2012).	↓ Plasma oxidative damage (mild heat; Costantini et al., 2012);↓catalase mRNA (liver), ↓NOX (liver, spleen and heart), ↑NOX (pectoralis), ↓SOD (spleen and heart)], ↑SOD (pectoralis) (Saleh et al., 2020).	↓ Catalase mRNA (spleen), ↓NOX mRNA (liver and spleen), ↓SOD (liver and spleen) (Saleh et al., 2020).
Metabolic rates	BMR (heat and cold, males; heat, females), PMR (heat and cold) (Wada et al., 2015), heat production (Moraes et al., 2003); basal oxygen consumption [Black & Burggren, 2004 (cold)].		↑ BMR (cold; females only; Wada et al., 2015)	↑ Total energy expenditure during hatching process [DuRant et al., 2011 (cold only)].	↑ Oxygen consumption during cold challenge [DuRant et al., 2012 (cold only)]; ↓ capacity to maintain oxygen consumption during cold challenge [Black & Burggren, 2004 (cold)].
Organ mass	Heart [Tzschentke and Halle, 2009; Shinder et al., 2009 (cold)]; liver [Yahav and Hurwitz, 1996; De Basilio et al., 2001; Tzschentke and Halle, 2009; Shinder et al., 2009 (cold)]; abdominal fat (De Basiolio et al., 2001; Collin et al., 2007); pectoralis (Collin et al., 2007; Tzschentke and Halle, 2009); gizzard (De Basilio et al., 2001; Tzschentke and Halle, 2009); spleen (Tzschentke and Halle, 2009); bursa (Liew et al., 2003).			↓ Heart (Yahav and Hurwitz, 1996; Yahav et al., 1997b); ↑heart [De Basilio et al., 2001; Shinder et al., 2011 (cold)]; ↑spleen (De Basilio et al., 2001); ↑pectoralis muscles [De Basilio et al., 2001; Piestun et al., 2011; Shinder et al., 2009, 2011 (cold)];↓abdominal fat [Yahav and Hurwitz, 1996; Piestun et al., 2011) (males)].	↓ Abdominal fat in females (Piestun et al., 2011).

Latent effect: Physiological changes that start to appear later in life, but which are sustained. Only after stress challenge: Effects that were only observed after the animal was challenged with a stressor later in life. Unless otherwise noted, these studies applied heat during the incubation or post-hatch period. Up and down arrows indicate an increase or a decrease relative to the controls. Gray boxes indicate effects that cannot be measured using current methods. No transgenerational effects were observed using developmental thermal stress. Empty cells indicate that this effect was not assessed.
HSP, heat shock protein; SOD, superoxide dismutase; NOX, NADPH oxidase. Other abbreviations as per Table 1.

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possible that a similar trade-off occurs in birds. If the proportion of certain organs relative to the body size differed between the control and stressed groups, these data would support the idea that developmental stressors change resource allocation among organ systems. However, current data on developmental thermal manipulation in birds show higher relative organ mass compared with controls for all organs measured or lower relative organ mass for all organs measured (De Basilio et al., 2001; Shinder et al., 2009; Yahav and Hurwitz, 1996; but see Piestun et al., 2011) (Table 2). Thus, there is currently no strong support for the trade-off hypothesis. For nutritional stress studies in birds, organ data are scarce, limiting our ability to determine whether there is a trade-off due to nutritional stress during development.

Gaps in knowledge and future directions

As we searched the literature, we found three categories of studies that underscored gaps in our current knowledge and an additional assumption made in these studies. One category of studies administered a stressor to animals during development and examined the effects on physiology and behavior (Fig. 1A). In this type of study, it is difficult to know if physiological changes ultimately increase the fitness potential of the individual. Thus, these studies likely do not encapsulate the full effect of the stressor on the individual.

The second category of studies administered a stressor to animals during development and examined the effects on physiology and behavior, and also included fitness correlates (Fig. 1B). Some studies in this category have used performance measures as a proxy for fitness potential. When fitness correlates are used, there are inherent assumptions that a certain body mass, body temperature and metabolic rate improve or reduce survival or reproductive success (Fig. 1). For instance, birdsong or plumage coloration is often used as an indicator of attractiveness in a male bird. However, very few studies have measured reproductive success such as fledging success along with birdsong. It is possible that female preference would change with developmental stressors and the current environment. Thus, whether stressed males with simpler songs are less successful at siring offspring is relatively unknown. Similarly, because the majority of thermal stress studies have been carried out in chickens, we know very little about how thermal stress affects song learning and production, female preference or reproductive success of the individual. It is important to note that if a developmental stressor tailored the animal towards a specific/stressful environment, measuring reproductive performance or survival in a benign environment could be misinterpreted. Thus, if at all possible, future studies should test more direct measures of reproductive success and fitness that may be affected by developmental stressors under various environments.

The third category of studies administered a stressor during development and again either later in life (the same or different stressor) or in the next generation and tested changes in stress tolerance – this type of study directly tests whether the developmental stressor causes adaptive phenotypic adjustment (Fig. 1C). When studies challenge animals later in life and quantify differences in mortality or reproduction between those exposed to a developmental stressor and controls, they can also inform us whether the developmental stressors in question bring fitness benefits in an equally stressful environment. However, studies where a stressor is applied later in life or in the next generation are rare, especially in nutritional stress studies. This may be the case in part because of a long generation time for most birds, limiting our ability to track long-term consequences and transgenerational effects. Although there are challenges in long-term experiments and logistical barriers of administering certain stressors, we urge researchers to test stress resistance and resilience (see Glossary) later in life.

Based on these gaps in knowledge, our recommendations for future studies are as follows. (1) Studies, whenever possible, should measure reproductive success (Andreasson et al., 2020) and/or survival to determine whether phenotypic adjustment due to the

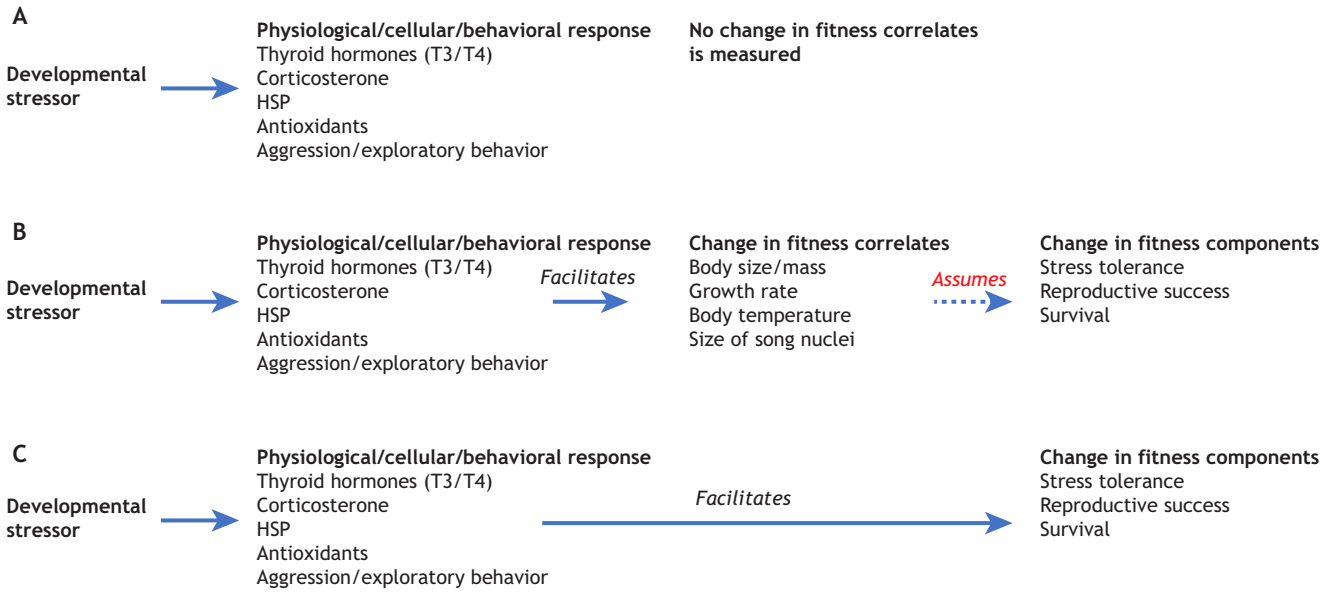

Fig. 1. Categories of developmental stress studies and their concepts. Our literature search found that the majority of studies of developmental stress in birds fell into one of three categories. (A) First, some studies examine the effects of suboptimal developmental environment on physiology, cellular processes or behavior. (B) Second, some studies assess fitness correlates such as body size and size of song nuclei in addition to physiology, cellular processes or behavior – this type of study identifies the mechanisms behind the observed changes in fitness correlates. It also makes assumptions that the fitness correlates predict changes in stress tolerance, reproductive success and survival. (C) The last type of study examines the physiological, cellular or behavioral changes and associated changes in fitness components.

environment experienced as young improves or impairs fitness components. Measuring fitness components also informs us which of the hypotheses listed above is more supported by the data. Importantly, measuring lifetime reproductive success through tracking the F3 generation ultimately determines how developmental stressors impact fitness of an individual. If measuring fitness components is not possible, authors should be clear about assumptions of measuring fitness correlates. (2) Assessing animals' reproductive success and survival under a stressor later in life will be an ultimate test for investigating whether phenotypic alteration is adaptive. If a developmental stressor does not enhance one's stress resistance and resilience, this likely confirms no adaptive response occurred. If a developmental stressor caused animals to thrive in a stressful environment, then further dose–response studies can quantify the range of stressor levels that induce an adaptive response by conditioning and the maximum performance and fitness gained by developmental stress exposure (Calabrese, 2013). At a minimum, we must keep in mind that the environment animals end up in during adulthood will likely influence the experimental results and interpretation of the results. (3) Measuring resource allocation such as the relative proportion of organ mass would test the trade-off theory. To allow multiple measurements of organ mass, we recommend using a non-invasive method (i.e. imaging or quantitative magnetic resonance) to examine whether (i) certain organs are shielded from the stressor more than others and (ii) the treatment effect on organ mass is transient or permanent. (4) Potential cross-tolerance between stressors is largely unknown. In poultry, restricting food during a period of heat stress improves the birds' ability to sustain body temperature and survival by reducing total heat load (reviewed in Abdel-Moneim et al., 2021). As developmental heat conditioning lowers body temperature for a prolonged period (Ncho et al., 2021), it is possible that such conditioning can alter nutritional handling later in life. Future studies should investigate stress tolerance of one stressor by exposure to another stressor during development. (5) Mixed results observed across nutritional and thermal stress may result from differences in stress manipulation in individual studies, particularly in nutritional stress studies. To resolve this, nutritional manipulation should be standardized depending on the research questions asked when possible. As the stress physiology field is urged to define 'stress' in each study and precisely describe what is manipulated (MacDougall-Shackleton et al., 2019), nutritional stress studies should also use language to reflect the treatment, such as caloric restriction, increased foraging, unpredictable food supply or lower food quality, to cluster studies by stressor and establish common patterns. (6) Both nutritional stress and thermal stress studies have strengths and shortcomings in their experimental approaches; adopting the strengths of nutritional stress studies can improve thermal stress studies, and vice versa. For instance, nutritional stress studies can take the robust factorial experimental designs used in thermal stress studies to expose animals to nutritional stress at another time point. Thermal stress studies can go beyond agricultural and laboratory model species and also assess the effects on behavior, cognition and sexually selected traits. When conducted in this way, new studies will help determine when developmental stressors induce adaptive responses.

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Competing interests
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Table S1. Overview of published effects of developmental nutritional manipulation on reproduction, fitness-related and behavioral variables.

[1]Changes that were observed long after the treatment was halted (although the variable in questions was measured only once)

[2]Effect that were only observed after the animal was challenged with a stressor later in life

[3]Effects observed in the subsequent generation

No latent or diminishing effects were observed using developmental nutritional stress.

Variable	No effect	Long-term effect[1]	Only after stress challenge[2]	Transgenerational[3]
		Birdsong		
Song parameters	duration (Brumm et al., 2009); duration of song motif (Noguera et al., 2017); number of song syllables, syllable types, song amplitude (Brumm et al., 2009); number of syllables in a song motif (Noguera et al., 2017); repertoire size (Nowicki et al., 2002); syllables copied from tutor (Brumm et al., 2009)	shorter song bouts directed, ↓mean song bouts undirected (Farrell et al., 2011); shorter songs, ↓ number of song syllables, ↓song peak frequency (Spencer et al., 2003); ↓time singing, took longer to start singing after song recording, fewer song bouts, shorter song bouts (Buchanan et al., 2003); ↑song rate (Honarmand et al., 2015); ↓song complexity (Noguera et al., 2017); ↓song repertoire (Spencer et al., 2004); sang sooner (Farrell et al., 2011; Nowicki et al., 2002); ↑ duration of subsong and early plastic stages, ↓song learning accuracy (Nowicki et al., 2002; Brumm et al. 2009)		
Song preference	HQ vs. LQ conspecific song (Farrell et al., 2015b)	↓time listening to conspecific song in early food removal, ↓time on perch associated with conspecific song in early food removal, ↓time listening to conspecific song in late food restriction, ↓time on perch associated with conspecific song in late food restriction (Farrell et al., 2015b)		
Song nuclei volume	HVC/telencephalon ratio (Nowicki et al., 2002); Farrell et al., 2015b	↓HVC, RA, telencephalon, RA/telencephalon ratio (Nowicki et al., 2002); ↓HVC (Buchanan et al., 2004)		
Zenk activation	between control and early food removal overall, early treatment when played heterospecific song, early food removal vs. late food-restricted females overall (Farrell et al., 2015b)	↓activation if late food restriction overall, ↓immunoreactive cells if played conspecific song in early food removal birds, ↓activation in control but late food-restricted when compared to pure controls; ↓NCMv activation compared to control regardless of playback song in early treatment (Farrell et al., 2015b)		

Variable	No effect	Long-term effect[1]	Only after stress challenge[2]	Transgenerational[3]
Behavior and cognition				
Emergence test	full emergence in offspring of treated birds (Ericsson et al., 2016)			↑latency until emerging in offspring of treated birds (Ericsson et al., 2016)
Tonic immobility	offspring of treated birds (Ericsson et al., 2016); offspring of treated birds (Goerlich et al., 2012)			
Open field test	activity in offspring of treated birds, latency to reinstate with social companions in offspring of treated birds (Goerlich et al., 2012); distance moved in offspring of treated birds (Ericsson et al., 2016)			↓time at the edges of the open field in offspring of the 8wk stress group, ↓latency to start moving in 8wk stress and 17wk stress (Ericsson et al., 2016)
Neophobia	Farrell et al., 2011; Kriengwatana et al., 2015; Zimmer et al., 2013	↑ escape attempts in early puberty group (Ericsson et al., 2016); ↓neophobia during sexual maturation (Noguera et al., 2015)		
Parental behavior	Krause et al., 2011			
Aggressiveness	Noguera et al., 2015			
Docility	Noguera et al., 2015			
Handling stress		↓response (Noguera et al., 2015)		
Boldness	Noguera et al., 2015			
Exploration	activity (Krause and Naguib, 2014); activity, exploration behavior (Krause and Naguib, 2015); latency to approach food, latency to feed, activity, number of huts visited, repeatability test (Krause and Naguib, 2011)	↓latency to approach food and latency to feed (Krause et al., 2009)		
Spatial foraging	Zimmer et al. 2013; latency to feed, mean number of visits throughout all trials at non-rewarding food sites prior to feeding, mean latency to leave start box (Krause et al., 2009); in juvenile nutritional treatment (Kriengwatana et al., 2015)	↓mean latency to approach food (Krause et al., 2009); ↓number of cups searched with early treatment (Kriengwatana et al., 2015)		
Learning	correct choice in offspring of treated individuals in associative learning (Goerlich et al., 2012); learning speed (Fisher et al., 2006); training duration, acquisition rate, number of days to reach criterion, and endpoint performance in auditory discrimination, duration of shaping, trials to criterion, and preservative errors in color discrimination (Farrell et al., 2016); reversal learning (Brust et al., 2014); spatial learning in juvenile-caught (Farrell et al., 2011)	↓ if strong compensatory growth response compared to control sibling (Fisher et al., 2006); ↑learning in color association, ↑learning in spatial association, ↓preservative errors in spatial assocation, ↑learning speed (Kriengwatana et al., 2015); ↓task acquisition in auditory discrimination, ↑within-trial errors in color discrimination (Farrell et al., 2016); ↑initial learning (Brust et al., 2014); ↑success in spatial learning tasks in nestling-caught, searched more cups and performed more errors in social learning (Farrell et al., 2011)		↑exploration of trees if parents LQ (Krause and Naguib, 2014); ↑offspring of treated individuals made a choice in associative learning (Goerlich et al., 2012)

Variable	No effect	Long-term effect[1]	Only after stress challenge[2]	Transgenerational[3]
Reproduction and survival				
Cheek patch development	Honarmand et al. 2010; at 35, 65, 280 dph (Krause and Naguib, 2015)	↓cheek patch growth, size at 35, and size at 50 dph (Krause and Naguib, 2015)		
Bill color		↓red (Noguera, 2017)		
Survival	Honarmand et al., 2010			
Offspring survival	Krause and Naguib, 2014		↓loss of red bill color with an enlarged brood (Noguera, 2017)	
Female mate choice	Honarmand et al., 2017; Honarmand et al., 2015	↓time with low quality males (Naguib and Nemitz, 2007)		
Male mate choice	Honarmand et al., 2017; for HQ male, no preference for HQ or LQ females (Noguera et al., 2017)	for LQ male, ↑ time with LQ females and ↑ active with LQ females (Noguera et al., 2017)		
Reproductive success	latency to egg laying, clutch size, hatching success, number of hatchlings (Honarmand et al., 2017); latency to egg laying, clutch size when LQ males paired with LQ females, clutch size when paired with HQ males regardless of treatment (Noguera et al., 2017)	↓ clutch size when LQ males paired with HQ females (Noguera et al., 2017)		

Table S2. Overview of published effects of developmental nutritional manipulation on growth and other physiological variables.

[1]Physiological changes that start to appear later in life, but which are sustained

[2]Changes due to a developmental stressor that diminish over time

[3]Changes that were observed long after the treatment was halted (although the variable in questions was measured only once)

[4]Effects observed in the subsequent generation

No effects that precipitated after a stress challenge were observed using developmental nutritional stress.

Variable	No effect	Latent effect[1]	Diminishing effect[2]	Long-term effect[3]	Transgenerational[4]
Growth and development					
Morphology	offspring of treated individuals at 11 and 56 dph (Ericsson et al., 2016); Noguera et al., 2015; body mass in males (Schmidt et al., 2012); body mass in early treatment (Kriengwatana et al., 2013); body mass at 0, 35, and 100 dph, tarsus at 17 dph (Krause and Naguib, 2014); body mass in treated males and female offspring of treated individuals (Goerlich et al., 2012); adult body mass (Noguera, 2017); wing chord, metatarsus, exposed culmen PCA (Chin et al., 2013)	↑body mass in females (Goerlich et al., 2012); ↑ change in body mass in ER/AL, AL/LR, and ER/LR (Chin et al., 2013); ↑growth rate after treatment end (Krause and Naguib, 2011); ↑body mass after treatment ended but before adulthood (Farrell et al., 2015a)	↓body mass and tarsus (Brumm et al., 2009; Honarmand et al., 2010); ↓Wing (took much longer; Brumm et al., 2009; Honarmand et al., 2010); ↓ body mass in females (Schmidt et al., 2012); ↓ body mass (Spencer et al., 2003); ↓body mass (Krause and Naguib, 2015); body mass in late food restriction (Chin et al., 2013); ↓ body mass (Fisher et al., 2006); ↓growth rate during treatment, ↓ body mass (Krause and Naguib, 2011); ↑body mass from after treatment until adulthood (Farrell et al., 2015a)	↑body mass (Buchanan et al., 2003; Farrell et al., 2011); ↓body mass (Krause et al., 2011); ↓body mass growth (Brust et al., 2014); offspring of HL and LH lighter than offspring of HH (Honarmand et al., 2017); ↑body mass in mismatched treatments and L juvenile treatment, ↑body mass in juvenile adult body mass, ↓body mass in HL females adult body mass, ↑body mass in juvenile treatment male adult body mass (Kriengwatana et al., 2013); ↓tarsus throughout the whole experiment (Krause and Naguib, 2015); ↓body mass in ER at 13 dph, ↓body mass in ER/AL, AL/LR, and ER/LR at 23 and 33 dph, ↓body mass in ER/AL and ER/LR in adulthood (Chin et al., 2013)	↓body mass at 17 dph, ↓tarsus in LL compared to the rest at 35 dph, ↓tarsus in LQ offspring treatment at 100 dph (Krause and Naguib 2014); ↑body mass in male offspring of treated individuals (Goerlich et al. 2012); ↑body mass of 17wk stress group's offspring at hatch, 8wk stress group's offspring at 28 dph compared to 2wk stress group's offspring (Ericsson et al. 2016)
Asymmetry	directional asymmetry, fluctuating asymmetry in alula feather (Pravosudov and Kitaysky, 2006)			↑ fluctuating asymmetry in tarsus, ulna, secondary flight feather (Pravosudov and Kitaysky, 2006)	
Body composition	adult total body mass, adult lean body mass, adult fat mass (Schmidt et al., 2012)	↑lean mass (Farrell et al., 2015a)	↓fat mass (Farrell et al., 2015a)		

Body size	Schmidt et al., 2012				
Body mass loss	Krause et al., 2009				
Body fat		↑males in juvenile treatment (Kriengwatana et al., 2013)		↓ in early treatment, ↑females in juvenile treatment (Kriengwatana et al., 2013)	
Other physiological responses					
Immune response	PHA, hematocrit (Buchanan et al., 2003); humoral immune response (Kriengwatana et al., 2013)			↓ humoral immune response (Buchanan et al., 2003); ↑antimicrobial activity juvenile, ↑HL than LL and HH in antimicrobial activity (Kriengwatana et al., 2013)	
Egg mass	Noguera et al., 2017			↑ egg mass (Goerlich et al., 2012); ↑in 2wk stress group (Ericsson et al., 2016)	