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ORIGINAL PAPER

Quantitative genetic evidence for trade-off between growth and resistance to oxidative stress in a wild bird

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Abstract Why do animals not grow at their maximal rates? It has been recently proposed that fast growth leads to the accumulation of cellular damages due to oxidative stress, influencing subsequent performances and life span. Therefore, the trade-off between fast growth and oxidative stress may potentially function as an important constraint in the evolution of growth trajectories. We test this by examining a potential antagonistic pleiotropy between growth and blood resistance to controlled free radical attack in a wild bird using a cross-fostering design and robust quantitative genetic analyses. In the yellow-legged gull *Larus michahellis*, decreased resistance to oxidative stress at age 8 days was associated with faster growth in mass, across the first 8 days of life, suggesting a trade-off between mass growth and oxidative-stress-related somatic maintenance. We found a negative genetic correlation between chick growth and resistance to oxidative stress, supporting the presence of the genetic trade-off between the two traits. Therefore, investment of somatic resources in growth could be constrained by resistance to oxidative stress in phenotypic and genetic levels. Our results provide first evidence for a potential genetic trade-off between life-history and underlying physiological traits in a wild vertebrate. Future studies should explore genetic trade-offs between life-history traits and other oxidative-stress-related traits.

Keywords Antagonistic pleiotropy · Heritability · Life-history evolution · Reactive oxygen species · Somatic growth · Trade-off

Introduction

Early growth is a critical period of life in most organisms, with strong effects on survival and reproductive performance during adulthood (Lindström 1999). In many species, fast growth can bring individuals a number of benefits and ultimately increase Darwinian

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fitness. Fast growing individuals, for example, may escape from the vulnerable early life stages as quickly as possible by attaining a larger body size and they may also reach a larger adult size and achieve sexual maturity at younger age, so potentially increasing their fitness by reducing generation times (Metcalfe and Monaghan 2003). However, animals normally do not grow at their maximal rate under given environmental conditions due to costs of accelerating growth, which may contribute to the variation in fitness that is not attributable to age or size at maturity (Dmitriew 2010). A number of studies have suggested that fast growth can have negative influences on fitness of individuals by reducing immune capacity, resistance to starvation during periods of food shortage and subsequent lifespan and by increasing predation risk and fluctuating asymmetry, and these have been confirmed in both laboratory and wild animals across diverse taxa (reviewed in Arendt 1997; Blanckenhorn 2000; Gotthard 2001; Metcalfe and Monaghan 2003; Dmitriew 2010). Therefore, fast growth potentially trades off other physiological and/or life-history traits and functions (Stockhoff 1991; Gotthard et al. 1994; Dmitriew 2010).

Growth is an integrated process, resulting in the response of cells dependent on the hormone and nutrient availability. Although the costs of rapid growth are typically thought of in relation to trade-offs in energy allocation, it has been recently proposed that growth leads to the accumulation of cellular damages, potentially affecting subsequent performances and life span (Mangel and Munch 2005). The "free radical theory of ageing" (Harman 1956), which originally proposed that endogenously generated reactive oxygen species (ROS) cause senescence via damage to DNA, lipids, and proteins (Beckman and Ames 1998; von Zglinicki 2002; Monaghan et al. 2009), provides a potential mechanism for negative influences of fast growth on physiological and life-history traits. Indeed, studies based on mammals suggested that fast growth can result in greater levels of oxidative damage (Merry 2000; Rollo 2002; Nussey et al. 2009), and a study of captive zebra finches *Taeniopygia guttata* showed that accelerated mass growth negatively affected the individual resistance to controlled free radical attack (Alonso-Alvarez et al. 2007). Oxidants are generated as a result of normal intracellular metabolism in mitochondria and peroxisomes as well as from a variety of cytosolic enzyme systems. Therefore, the generation of ROS becomes a function of metabolic rate, and the rate of metabolism can be positively related to the rate of oxidative stress (Harman 1956; Finkel and Holbrook 2000). However, it has also been observed that individuals with high metabolic rates have greater mitochondrial uncoupling, which should lead to lower ROS and longer life span (Brand 2000; Speakman et al. 2004). Fast metabolism required for rapid growth could generate oxidative stress at cellular levels by increasing membrane and mitochondrial-derived free radicals (Beckman and Ames 1998; Rollo 2002) as shown in studies of cellular senescence (e.g., Wei et al. 1998; Jennings et al. 2000). Therefore, trade-offs between fast growth and the balance between ROS generation and antioxidant systems may potentially function as an important constraint in the evolution of growth trajectories.

Evolutionary theory is concerned with genetic processes, but is often tested with data collected on phenotypes, assuming that phenotypic patterns are good predictors of the underlying genetics ("phenotypic gambit"; Grafen 1984). However, the generality of this assumption remains controversial, particularly for traits with low heritabilities such as life-history and physiology because genetic influences on the phenotypic patterns are relatively minor, compared to environmental influences (Hadfield et al. 2007). Most studies based on laboratory animals examined the negative phenotypic effects of fast growth by correlating growth in mass to antioxidant status, oxidative damage or susceptibility to oxidative stress (Rollo 2002; Alonso-Alvarez et al. 2007). However, the sources underlying the phenotypic correlations between growth and oxidative-stress-related traits remain poorly understood.

Examining genetic correlations between growth and oxidative-stress-related traits may allow us to understand the correlated response of these traits to directional selection and the presence of potential genetic trade-offs among them (Roff 2002).

In the present study, we examined phenotypic and genetic correlations between growth and blood resistance to controlled free radical attack. Both growth and resistance to oxidative stress are fitness-related traits (Metcalfe and Monaghan 2003; Alonso-Alvarez et al. 2006). Growth is often heritable (Gebhardt-Henrich and van Noordwijk 1991; Arendt 1997; Starck and Ricklefs 1998; Roff 2002) and some oxidative-stress-related traits also have a genetic basis (Holzenberger et al. 2003; Olsson et al. 2008; Paaby and Schmidt 2009; Kim et al. 2010b). Here, we measured blood resistance to controlled free radical attack as a parameter of quantitative genetic analyses because it reflects the efficiency of an organism's cellular defense against ROS damage (Alonso-Alvarez et al. 2006; Bize et al. 2008), which is largely determined by the genotype (Kim et al. 2010b). Blood resistance to free radical attack is shaped by membrane lipid composition and past exposure of unsaturated lipid bonds to oxidative stress as well as by levels of intra- and extra-cellular antioxidant defenses (Bize et al. 2008).

Here, we first examined the relationship between resistance to controlled free radical attack and growth, and then explored genetic and environmental sources of the phenotypic correlations between chick growth and resistance to oxidative attack in yellow-legged gull *Larus michahellis* chicks. We used cross-fostered gull chicks to disentangle similarities in the resistance to oxidative attack and growth within broods due to genetic influences and shared environments (Rubolini et al. 2006). Using robust statistical procedures, we explored the phenotypic, genetic, and environmental correlations between early growth and blood resistance to controlled free radical attack. Positive phenotypic and genetic correlations can be expected if genes encoding for effective antioxidant machinery would allow individuals to grow fast, whereas negative correlations would be expected if a phenotypic and genetic trade-offs exist between the two traits. Finally, we discuss the potential role of oxidative stress in the evolution of growth. This is the first study to our knowledge that examines a potential genetic trade-off between physiological and life-history traits in a wild vertebrate.

Materials and methods

Study system and general field procedures

We carried out this study from May to June 2009 at a colony of yellow-legged gulls in the Parque Nacional das Illas Atlánticas, Sálvora Island, Galicia, Spain (42°28′N, 09°00′W). Yellow-legged gulls lay eggs generally at 1- to 3-days interval to complete a clutch of three eggs (modal clutch size), and incubation and parental care for chicks are shared by both parents. The semi-precocial young hatch asynchronously, with the third chick hatching normally 1–3 days after the other two (Hillström et al. 2000).

We surveyed the study areas once daily during egg laying, and marked new nests with numbered bamboo sticks. We visited each nest until clutch completion, and marked eggs individually on the day of laying with a permanent marker. A total of 72 nests with a clutch of three eggs were used for this study. To disentangle genetic and environmental (co)variances of chicks in resistance to oxidative stress and growth, all three eggs were swapped 1 day after clutch completion within a group of four nests in which the second and third eggs were laid on the same days (at 2-days interval). This resulted in all three

eggs from the same original nest being incubated (then the hatchlings being raised) in three different recipient nests other than the original nest, but conserving their original laying order within the clutch.

We checked each nest daily beginning 2 days before the estimated hatching date (28 days after laying date) until all the chicks were hatched. A total of 191 chicks hatched among the 72 study nests. All the third chicks (from eggs laid in the third position) hatched 1–3 days later than their foster-siblings or the fastest on the same day as their foster-sib(s). Therefore, cross-fostering experiment did not change natural order of hatching within the recipient broods. We marked all hatchlings using leg flags made with colored Velcro on the day of hatching (day 0) for their identification. All chicks were weighed and measured at day 0, 2, 5 and 8 and blood sampled at day 0 and day 8 of age. A total of 118 chicks were recaptured at age 8 days for measurement and blood sampling (see below). We measured resistance to controlled free radical attack at day 8 because at this time basal metabolism is close to the peak after an exponential increase in gull chicks (Drent et al. 1992). We weighed chicks to the nearest 0.01 g using electronic balances or to the nearest 1 g using spring balances, and measured tarsus length to the nearest 0.01 mm using electronic calipers.

Growth parameter

Tarsus length and mass measured at day 0, 2, 5 and 8 showed linear increases in the study chicks (our unpublished data). Therefore, linear growth rates in mass and tarsus length from hatching to day 8 were used for analysis. Oxidative stress is expected to constrain body mass growth but not skeletal growth. Muscle growth and adipose tissue deposition are more metabolically demanding activities (e.g., Moe et al. 2004; Vézina et al. 2009), compared with skeletal growth, which is more affected by cellular transduction systems (e.g., Tatara 2008). In birds, body mass is a good predictor of basal metabolic rates (Hulbert et al. 2007), and growing fat can be costly due to mass-dependent metabolic expenditure (Dietz and Drent 1997). In contrast, skeletal growth (cell proliferation) may reduce oxidative stress through a reduced protein turnover (McCarthy et al. 1994; Samuels and Baracos 1995; Rollo 2002). However, since growth in skeletal size and mass are strongly correlated in birds (Schulte-Hostedde et al. 2005), it is difficult to disentangle their biological aspects. Indeed, body mass growth and skeletal size growth were significantly related in the study chicks (see Results). Therefore, skeletal growth rate in tarsus length was taken into account as a covariate in the analysis of mass growth rate.

Measurement of blood resistance to oxidative stress

To assess blood resistance to oxidative stress and hematocrit (and for molecular sexing, see below), we collected blood from the leg or wing vein of each chick on the day of hatching (0.05–0.1 ml) and day 8 (0.2–0.3 ml) using a sterile needle and heparinized capillary tubes. 20 µl of whole blood were mixed with 730 µl of saline buffer adapted to avian physiological parameters (158 mM Na^+, 144 mM Cl^-, 6 mM K^+, 24 mM HCO_3^-, 2 mM Ca^{2+}, 340 mOsm, pH 7.4) immediately after blood sampling. The sample mixed with the saline buffer and the rest of the blood were stored at 4°C before analysis of resistance to oxidative stress and hematocrit, respectively, that occurred within 10 h.

Resistance to oxidative stress was assessed as the time needed to hemolyze 50% of red blood cells exposed to controlled free-radical attack (see also Alonso-Alvarez et al. 2006) for all hatchlings and 115 chicks of age 8 days. Among the chicks recaptured at age 8 days,

two were not blood sampled due to extremely bad body conditions and one chick's sample was inadequate for analysis due to abnormally high proportion of protein in the whole blood.

Each blood sample mixed with the saline buffer was added in two wells (for duplicated analysis, 80 μl per well) of a 96-well microplate, then 136 μl of a 150-mM solution of 2,2′-azobis-(aminodinopropane)hydrochloride [AAPH] diluted in saline buffer was subsequently added to each well. The microplate was incubated at 40°C until all samples reach to their minimum values (3–4 h) while the hemolysis of red blood cells was assessed with a microplate reader, which measures the decrease of optical density at the wavelength of 540 nm (see Alonso-Alvarez et al. 2006, 2007 for details), every 10 min. To test whether concentration of red blood cells influences time needed to hemolyze, hematocrit value was determined by centrifuging a capillary tube filled with whole blood sample and measuring the proportion of blood volume occupied by packed cells for each individual at day 8. However, resistance to oxidative stress was not related to hematocrit value in the study chicks ($N = 115$, $r = 0.126$, $P = 0.179$). Therefore, hematocrit value was not taken into account in the subsequent statistical analyses.

Sex identification of chicks

To identify the sex of the chicks, a droplet of blood collected from each chick on the day of hatching was mixed with alcohol and stored at room temperature until molecular sexing at a laboratory (IREC-CSIC, Spain). Chick sex was identified from blood cell DNA by detecting two CHD genes (CHD1W and CHD1Z), using a pair of primers (2550F and 2718R) (Fridolfsson and Ellegren 1999).

Statistical analyses

We examined factors associated with mass growth rate of chicks using a standard linear mixed-effect model (LME), including original and recipient nests as random effects to account for the non-independence of chicks from the same original and/or recipient brood. Initially a LME with all explanatory variables and two-way interactions of interest were fitted for mass growth rate using a maximum-likelihood (ML) algorithm [full model: mass growth rate = chick position + sex + hatching date + initial mass (day 0) + tarsus growth rate + resistance OxStress (day 0) + resistance OxStress (day 8) + position × resistance OxStress (day 8) + sex × resistance OxStress (day 8)]. Then non-significant interactions and main terms were dropped sequentially to simplify the model. The significance of the removal of each term was tested using a likelihood ratio test based on log-likelihoods obtained from the LMEs (Crawley 2007). This model simplification method proceeded until we obtained a minimum adequate LME that includes only terms significant at the $P < 0.05$ level (Crawley 2007). Analyses were carried out using R version 2.10.1 (R Development Core Team 2009).

Heritabilities, common environmental effects, and trait correlations for chick growth in mass and resistance to oxidative attack at day 8 were estimated using a REML bivariate mixed-effect model in ASreml version 2 (VSN International; Gilmour et al. 2006). Genetic and common environmental (co)variances for the two traits were estimated by fitting original and recipient nests as random effects in the bivariate model (see also Kim et al. 2010a). Mass growth rate was significantly correlated to chick position, hatching date and tarsus growth rate (see Results, Table 1) while exploratory analysis showed that only hatching date had significant influence on resistance to oxidative attack ($P = 0.01$; see also

Table 1 Summary of minimum adequate LME fitted using REML for mass growth rate (g/day) in yellow-legged gull chicks ($N = 115$)

Random effects	Variance (±SD)			
Original nest	1.125 ± 1.061			
Recipient nest	1.549 ± 1.245			
Residual	4.798 ± 2.190			
Fixed effects	**Estimate (±SE)**	χ^2	*df*	*P*
(Intercept)	−23.239 ± 8.010			
Position first	0	7.596	2	0.022
Second	0.027 ± 0.511			
Third	−1.770 ± 0.684			
Hatching date	0.805 ± 0.228	12.405	1	<0.001
Tarsus growth rate (mm/day)	9.633 ± 0.852	84.547	1	<0.001
Resistance OxStress (day 8)	−0.083 ± 0.033	5.984	1	0.014

Original and recipient nests were fitted as random effects in the model

Full model: mass growth rate = chick position + sex + hatching date + initial mass (day 0) + tarsus growth rate + resistance OxStress (day 0) + resistance OxStress (day 8) + position × resistance OxStress (day 8) + sex × resistance OxStress (day 8)

Kim et al. 2010b). Therefore, chick position, hatching date, and tarsus growth rate were included as fixed effects in the bivariate model fitted to mass growth and resistance to oxidative attack. Additive genetic (co)variances (V_A and Cov_A) were calculated as twice the (co)variance component of original nest (V_{Origin} and Cov_{Origin}) because full siblings share 50% of their genes (Lynch and Walsh 1998). Note that extra-pair paternity is very rare in gulls (Bukacinska et al. 1998; Gilbert et al. 1998). Environmental (co)variances (V_E and Cov_E) were equal to the recipient nest component ($V_{Recipient}$ and $Cov_{Recipent}$), and phenotypic variances were calculated as the sum of the original nest, recipient nest and residual variance components ($V_P = V_{Origin} + V_{Recipient} + V_R$). Narrow sense heritability (h^2) and common environmental effect (c^2) were estimated as $h^2 = V_A/V_P$ and $c^2 = V_E/V_P$ for each trait. Phenotypic, genetic and environmental correlations (r_P, r_A and r_E) between the two traits were also estimated. The statistical significance of each covariance was assessed using likelihood ratio tests that compare models based on −2 times the difference in REML log-likelihood scores distributed as χ^2. Models were reduced by fixing covariance parameters of the random effects to zero, and the degrees of freedom equaled the number of covariance constrained to zero. The significance of each variance component function was assessed using a two-tailed *t* test.

Results

Variation in chick growth rate in mass from hatching to day 8 was explained by chick position (egg laying order), hatching date, growth rate in tarsus length, and blood resistance to controlled free radical attack at day 8 (Table 1). The third chicks grew slower than the first and second chicks, and hatching date and growth rate in tarsus were positively related to growth rate in mass (Table 1). Chicks with lower blood resistance to oxidative stress at

day 8 grew faster in mass from hatching to day 8 when the effects of chick position, hatching date, and tarsus growth rate were taken into account (Fig. 1). Other terms, sex, resistance to oxidative stress at hatching (day 0), position × resistance oxidative stress (day 8), and sex × resistance to oxidative stress (day 8), were non-significant.

A significant proportion of the total phenotypic variance for resistance to oxidative attack at day 8 was explained by original nest effects, leading to high and significant heritability, but the recipient nest of the chicks did not influence the phenotypic variation (Table 2). These results from the bivariate mixed-effect model were consistent with the results based on a univariate mixed-effect model (Kim et al. 2010b; $h^2 = 0.59 \pm 0.25$, $P = 0.01$; $c^2 = 0.11 \pm 0.11$, $P = 0.18$). Chick growth in mass showed high heritability and recipient nest effect, but these were non-significant due to large standard errors (Table 2).

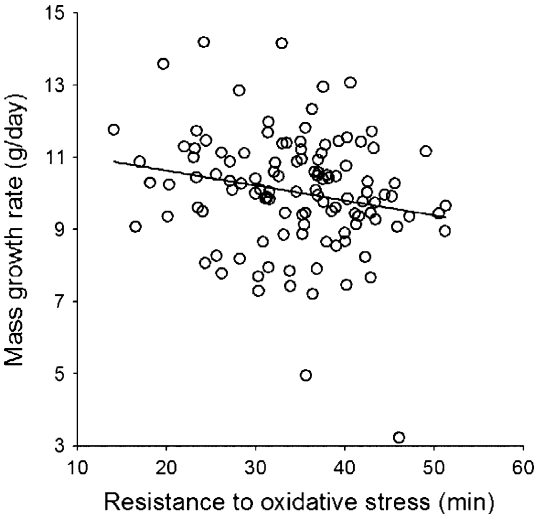

Fig. 1 Relationship between blood resistance to oxidative stress at day 8 (min) and mass growth rate from hatching to age 8 days (g/day). The presented values for mass growth rate are residuals from the LME (mass growth rate = chick position + hatching date + tarsus growth rate; see Table 1) + trait mean (mean ± SE: 10.038 ± 0.390 g/day, $N = 115$). The *fitted line* is a *linear* regression ($r = -0.202$)

Table 2 Quantitative genetics on resistance to oxidative stress at day 8 (min) and chick growth in mass (g/day) from a REML bivariate mixed-effect model ($N = 115$)

Statistic	Resistance to oxidative stress	Chick growth
$h^2 \pm$ SE	0.59 ± 0.25 ($P = 0.018$)	0.41 ± 0.25 ($P = 0.105$)
$c^2 \pm$ SE	0.09 ± 0.11 ($P = 0.433$)	0.24 ± 0.13 ($P = 0.057$)
$Cov_P \pm$ SE	-7.06 ± 2.43 ($P < 0.001$)	
$Cov_A \pm$ SE	-9.07 ± 4.67 ($P = 0.039$)	
$Cov_E \pm$ SE	-3.81 ± 2.15 ($P = 0.062$)	
$r_P \pm$ SE	-0.30 ± 0.09 ($P < 0.001$)	
$r_A \pm$ SE	-0.79 ± 0.35 ($P = 0.026$)	
$r_E \pm$ SE	-1.12 ± 0.72 ($P = 0.123$)	

The quantitative genetic parameters reported are heritability (h^2), common environmental effect (c^2), phenotypic, additive genetic and environmental covariances (Cov_P, Cov_A and Cov_E) and correlations (r_P, r_A and r_E)

Chick position, hatching date, and tarsus growth rate were included as fixed effects in the bivariate model

Corresponding significances are reported within brackets

Our results from the bivariate model showed significant negative phenotypic and genetic correlations between chick growth and resistance to oxidative stress (Table 2). Thus, families showing relatively fast growth in mass during the early nestling periods were those with low resistance to oxidative stress.

Discussion

In the yellow-legged gull, a potential trade-off between resistance to oxidative stress and growth rate in mass during the early nestling periods was observed. Chicks with decreased resistance to controlled free radical attack at day 8 grew faster in mass from hatching to day 8. Both blood resistance to oxidative attack and chick mass growth showed high heritable variances ($h^2 = 0.59$ and $h^2 = 0.41$, respectively), although this was significant only in blood resistance. However, the rearing environment of chicks had low and non-significant effects on phenotypic variances of the two traits, although it is likely that importance of the common environmental effects increases as chicks grow. Our quantitative genetic analyses suggest that the negative phenotypic correlation between chick growth and resistance to oxidative attack potentially has a genetic basis as shown by a significant negative genetic correlation between the two traits.

Conditions in very early life may alter the balance between ROS production and antioxidant defense and repair capacity (Monaghan et al. 2009; Nussey et al. 2009; Hall et al. 2010). It is particularly true for vertebrates that experience profound change in aerobic conditions and a potential oxidative insult at hatching or birth (Surai 2007). Gull chicks develop precocially but grow rapidly after hatching (Ricklefs 1979), and the increase in metabolic activity needed to fuel rapid growth may cause oxidative damage to the organism (Rollo 2002; Alonso-Alvarez et al. 2007). In the present study, growth in mass during the early nestling period (from hatching to day 8) was negatively correlated to resistance to oxidative attack at day 8 across all chicks from different laying positions. Our result suggests the presence of oxidative costs to early growth as would be predicted by life-history theory (Stearns 1992) and thereby a potential trade-off between growth and oxidative-stress-related somatic maintenance (Nussey et al. 2009). In the study chicks, mass growth was not related to resistance to oxidative stress at hatching, suggesting that growth was independent to antioxidant defense and repair capacity in very early life. In birds, rapid mass growth trades off immunological competence (Soler et al. 2003) and blood resistance to oxidative stressors (measured in the same method as the present study; Alonso-Alvarez et al. 2007). During early development, chicks accumulate subcutaneous and internal fat and increase skeletal muscle mass (Øyan and Anker-Nilssen 1996; Schew and Ricklefs 1998). Accelerated mass growth promotes increased metabolic rates (Vleck and Vleck 1980; Drent et al. 1992; Dietz and Drent 1997), leading to the more severe oxidative-stress-related cellular damage (Loft et al. 1994; Rollo et al. 1996; Morgan et al. 2000). Thus, rapid growth in mass early in life may give rise to a subsequent penalty in somatic maintenance (Metcalfe and Monaghan 2001), as shown in our results of the negative relationship between cellular resistance to a radical attack and chick growth. Nevertheless, the negative correlation between resistance to oxidative stress and growth should be further explored by examining oxidative damages on lipids, proteins and DNA (Monaghan et al. 2009).

The trade-off between growth and resistance to oxidative attack at the phenotypic level can be explained as a consequence of oxidative costs of increased investment in growth resulted from diversion of limited somatic resources away from somatic maintenance

(Stearns 1992). Furthermore, the negative phenotypic correlation between growth and resistance to oxidative attack suggests a potential antagonistic pleiotropy (i.e., genetic trade-off) that occurs when a gene has a positive effect on one trait but a negative effect on another. However, a phenotypic correlation solely is not sufficient to demonstrate that there is a genetic trade-off between traits (Cotter et al. 2004). Our result of the negative genetic correlation between growth and resistance to oxidative stress during the early nestling periods in gulls supports the presence of the genetic trade-off between the two traits. Blood resistance to oxidative stress represents the individual antioxidant capacity to mitigate damaging effects of ROS. Recent molecular studies have shown that resistance to a ROS-induced hemolysis and regulations of postnatal growth rates possibly have genetic bases in mammals (Ito et al. 2004; Lui et al. 2008). Some of the genes involved in antioxidant machinery and ROS production of organisms may play a role in regulation of cell proliferation and somatic growth. For example, genes regulating mitochondrial functions should influence both somatic metabolism required for growth and ROS production (Dillin et al. 2002; Hulbert et al. 2007). Other candidate genes could be eukaryotic initiation factor 2Bδ (*eIF2B*δ/F11A3.2); its expression increases fat storage, but reduces oxidative stress resistance (Tohyama et al. 2008). Alternatively, the negative genetic correlation between resistance to oxidative stress and growth may be due to linkage disequilibrium. Linkage disequilibrium occurs when two traits are affected by distinct gene loci but some evolutionary force, which correlates trait combinations, creates and maintains a non-random association between the alleles (Falconer and Mackay 1996). However, under normal levels of recombination, linkage between rapid growth and low resistance to oxidative stress is unlikely because these traits are positively related to fitness.

In birds, estimates of genetic effects may be inflated due to maternal investment into eggs. This possibility should be considered because maternal antioxidants and hormones allocated into eggs can influence oxidative stress and post-natal growth in chicks (Eising et al. 2001; Rubolini et al. 2006; Surai 2007). In the study chicks, resistance to oxidative stress at day 8 was not related to resistance measured at hatching, suggesting that antioxidant defense and repair capacity during the growth may be independent to those in very early life (i.e., at hatching; Kim et al. 2010b). Moreover, there was no effect of plasma antioxidants on blood resistance to oxidative stress in our study chicks during the early nestling periods (i.e., at hatching; Kim et al. 2010b), suggesting that maternally derived antioxidants in eggs probably have rather weak influences on the similarity in oxidative conditions among genetic siblings during the post-natal growth. However, it does not exclude the possibility of indirect maternal effects on blood resistance to oxidative stress through hormones. More complex experiments are required to disentangle the maternal influences from genetic (co)variance in full-sibling models (e.g., Pitala et al. 2007).

In conclusion, our results suggest that oxidative costs can limit growth rates in body mass in natural populations. The negative genetic correlation between growth and resistance to oxidative stress provides a framework to explain the role of oxidative stress in growth trajectories, although our understanding is still immature and evidence is limited. Theoretical and empirical studies have suggested that the organism's capacity to mitigate oxidative stress is likely to be a major determinant of life-histories such as reproduction, senescence and life span (reviewed in Monaghan et al. 2009; Dowling and Simmons 2009; Kim et al. 2010a) and thereby fitness. Therefore, investment of somatic resources in growth should be constrained by resistance to oxidative stress. The potential genetic trade-off between growth and resistance to oxidative attack provides compelling support for the role of oxidative stress in the evolution of growth. Furthermore, the negative genetic correlation between growth and resistance to oxidative stress may explain how genetic variations for

the two traits have been maintained despite selection in wild populations. The genetic trade-off between the two traits may constrain any response to selection and can also play a fundamental role in the maintenance of genetic variation in the traits under selection (Roff 1992).

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