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Report

Evidence for a Genetic Basis of Aging in Two Wild Vertebrate Populations

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Summary

Aging, or senescence, defined as a decline in physiological function with age, has long been a focus of research interest for evolutionary biologists. How has natural selection failed to remove genetic effects responsible for such reduced fitness among older individuals? Current evolutionary theory explains this phenomenon by showing that, as a result of the risk of death from environmental causes that individuals experience, the force of selection inevitably weakens with age [1–3]. This in turn means that genetic mutations having detrimental effects that are only felt late in life might persist in a population. Although widely accepted, this theory rests on the assumption that there is genetic variation for aging in natural systems [4, 5], or (equivalently), that genotype-by-age interactions (GxA) occur for fitness. To date, empirical support for this assumption has come almost entirely from laboratory studies on invertebrate systems, most notably *Drosophila* and *C. elegans* [6–10], whereas tests of genetic variation for aging are largely lacking from natural populations [5]. By using data from two wild mammal populations, we perform quantitative genetic analyses of fitness and provide the first evidence for a genetic basis of senescence to come from a study in the natural environment. We find evidence that genetic differences among individuals cause variation in their rates of aging and that additive genetic variance for fitness increases with age, as predicted by the evolutionary theory of senescence.

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Results and Discussion

We examined the additive genetic basis of variation in aging rates by using data from two long-term studies of wild ungulates, Soay sheep (*Ovis aries*), and red deer (*Cervus elaphus*) from the Scottish islands of Hirta (St. Kilda) and Rum, respectively [11, 12]. The systems are ideal for this purpose because they provide unparalleled levels of data (including individual survival and reproductive success) for large numbers of long-lived animals. In both study systems, individually marked animals are followed throughout their lives from birth until death. Furthermore, pedigree structures elucidated with a combination of observational and molecular approaches allow the application of quantitative genetic models to data.

Although genetic studies of senescence have often tended to focus on mortality, evolutionary theory relates specifically to the age-specific probabilities of both survival and reproduction [13, 14]. Here, we have used an annual measure of individual fitness (p_{ti}) that describes an individual's contribution to annual changes in population size [15–17] (p_{ti}; see Experimental Procedures). This measure consequently incorporates contributions from both survival and annual breeding success. In females of both species, average annual fitness shows a strong signature of senescence (Figure 1). Thus, the age-specific mean initially increases from birth (to a maximum at age 4 years in sheep and age 8 years in deer) before declining in old age. Although age effects on survival are well known [18, 19], the consideration of contributions from survival and fecundity separately (data not shown) reveals that reproductive senescence also occurs in these populations.

We used quantitative genetic animal models [20] to test whether variation in aging rates in annual fitness in female red deer and Soay sheep had an additive genetic basis and to explore how additive genetic (co)variance in fitness changed with age in these populations. Animal models use available pedigree structures to partition phenotypic variance into additive genetic and environmental effects. We began by splitting annual fitness data from each population into discrete age classes (lambs, yearlings, 2–4 year olds, and $\geq$ 5 year olds for the Soay sheep; yearlings, 2 year olds, 3–8 year olds, and $\geq$ 9 year olds for the deer, see Experimental Procedures) and testing whether additive genetic variation for fitness differed between age classes. We then applied random regression animal models [21, 22] to the full deer and sheep data sets. These models allowed us to specifically test for additive genetic variation in individual aging rates and to generate predicted age-specific additive genetic (co)variance matrices (**G** matrices) across all ages without the dramatic loss of power associated with subdividing the data into age classes (see Experimental Procedures; [22]).

There was evidence of age-specific genetic effects on fitness in both red deer and Soay sheep populations.

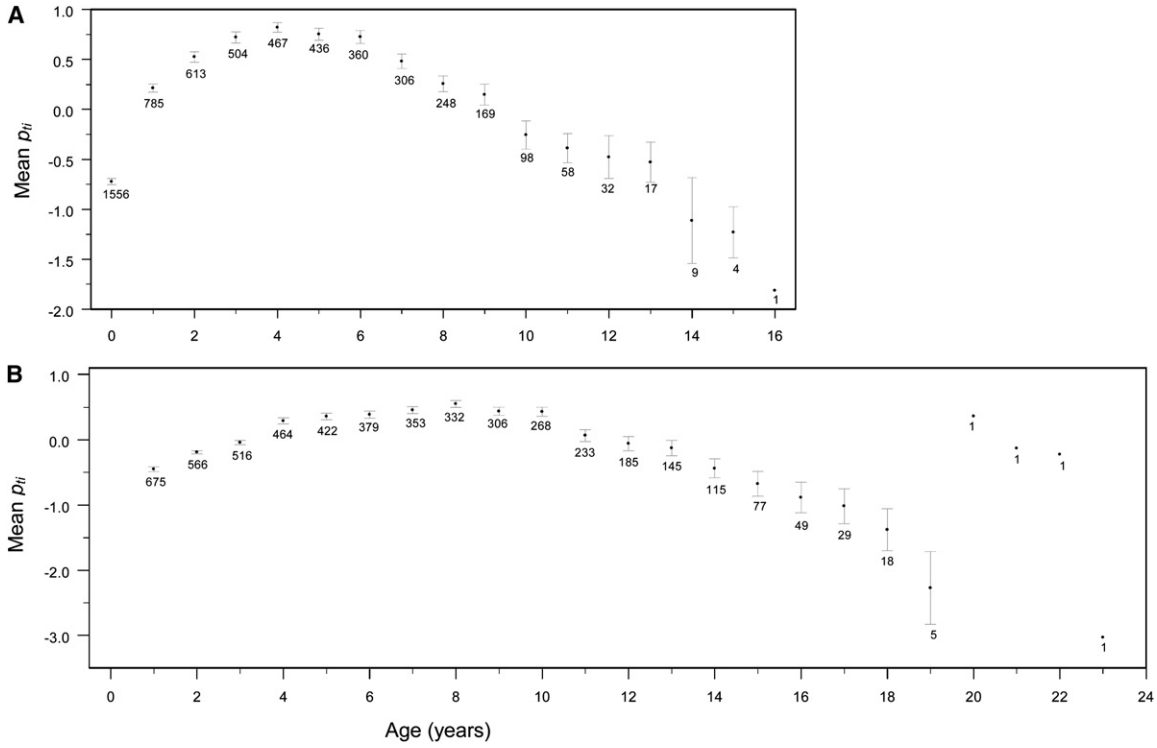

Figure 1. Age-Specific Average Fitness in Soay Sheep and Red Deer

Plots of mean annual fitness p_{ti} by age (in years) in female (A) sheep and (B) deer. Error bars indicate ± the standard error (SE). Note that p_{ti} incorporates fitness contributions from both survival and reproductive success, but the latter is defined slightly differently in the two systems (see Experimental Procedures).

Analyses of additive genetic variance for fitness in different age classes suggested that additive genetic variance (σ^2_A) for fitness varied over ontogeny. In particular, estimated additive variance was greater in the oldest data subsets than in prime-age animals for both sheep and deer (Table 1). We used bivariate formulations of Model 1 (see Experimental Procedures) to test the significance of these differences. In red deer, σ^2_A was three times greater in the older (9+) females than in prime-age animals, a difference that was statistically significant ($\chi^2_1 = 5.36$, $p = 0.02$). In Soay sheep, significant additive genetic variance for fitness was only found for the 5+ females. In contrast, for prime-age sheep, σ^2_A was estimated as −0.013 (±0.065) and fixed at zero with the model constrained to positive parameter space (Table 1). Although we interpret these results as indicating an absence of genetic variance in prime age, it should be noted that under an (unconstrained) bivariate model, there was no significant difference between σ^2_A in prime-age and older sheep ($\chi^2_1 = 2.6$, $p = 0.11$).

Random regression animal models [21–23] also supported the presence of additive genetic variance in aging rates (or significant GxA). In both populations, under Model 2 (in which residual variance was assumed to be constant with age) the presence of GxA was statistically supported (likelihood-ratio tests: Soay sheep $\chi^2_2 = 7.18$, $p = 0.028$; red deer $\chi^2_2 = 126$, $p < 0.001$). We were also able to parameterize random regression animal models by using heterogeneous error structures (Model 3, see Experimental Procedures for details), providing significantly better fits in the Soay sheep ($\chi^2_{10} = 44.6$, $p < 0.001$) and red deer ($\chi^2_{14} = 389$, $p < 0.001$). Under this more complex model, the GxA interaction was still highly significant in red deer (likelihood-ratio comparison of models with $x = 0.1$; $\chi^2_2 = 12.7$, $p = 0.002$). However, in Soay sheep, the GxA interaction was no longer statistically significant (likelihood-ratio comparison of first order and constant models: $\chi^2_2 = 1.20$, $p = 0.549$). This suggests that Model 2 might be subject to bias (e.g., by increasing residual variance with age). However, age-specific estimates of the additive variance (discussed below) were similar under models 2 and 3 (Figures 2A and 2C), and it is also likely that power limitations under the more complex model contribute to a lack of significance. In order to determine how GxA influences the expression of genetic variance at different ages, the full **G** matrices of for annual fitness were reconstructed from Model 3 in both populations. However, before discussing their structure, we reiterate that GxA was significant only in red deer such that and age-related patterns in Soay sheep must be considered suggestive only.

In both red deer and Soay sheep systems, estimated σ^2_A increased with age, whereas genetic correlations declined as the time between measurement ages increased (Figures 2 and 3). The observed increase in σ^2_A in late life is predicted by the evolutionary theory of aging, as a consequence of mortality leading to weakening selection with age [2, 4, 5]. Selection on alleles with deleterious effects in late life is expected to be weak because comparatively few individuals survive long enough for the effects to be expressed. Furthermore, the rescaling of the full covariance matrices (Tables S1 and S2 available online) showed that although genetic

Table 1. Components of Variance in Annual Fitness for Age-Specific Subsets of Soay Sheep and Red Deer

Population	Age Class	Mean (SE)	σ^2_P	σ^2_Y	σ^2_{PE}	σ^2_M	σ^2_R	σ^2_A	P
Soay Sheep									
	Lambs	−0.723 (0.030)	1.448 (0.056)	0.052 (0.023)	nf	0.092 (0.041)	1.246 (0.069)	0.059 (0.059)	0.217
	Yearlings	0.107 (0.041)	1.343 (0.069)	0.021 (0.02)	nf	0.000 (-)$^+$	1.161 (0.119)	0.161 (0.111)	0.161
	Prime age (2–4)	0.670 (0.031)	1.493 (0.061)	0.062 (0.026)	0.367 (0.056)	0.000 (-)$^+$	1.065 (0.052)	0.000 (-)$^+$	1
	Older (5+)	0.498 (0.033)	1.581 (0.059)	0.04 (0.02)	0.054 (0.068)	0.000 (-)$^+$	1.342 (0.054)	0.145 (0.071)	0.035
Red Deer									
	Yearlings	−0.449 (0.037)	0.953 (0.053)	0.002 (0.011)	nf	0.00 (-)$^+$	0.817 (0.085)	0.135 (0.081)	0.070
	Second years	−0.190 (0.024)	0.320 (0.025)	0.061 (0.019)	nf	0.000 (-)$^+$	0.259 (0.016)	0.000 (-)$^+$	1
	Prime age (3–8)	0.307 (0.020)	0.939 (0.027)	0.006 (0.005)	0.000 (-)$^+$	0.002 (0.012)	0.880 (0.028)	0.050 (0.019)	0.015
	Older (9+)	0.016 (0.037)	1.760 (0.073)	0.017 (0.014)	0.000 (-)$^+$	0.000 (-)$^+$	1.593 (0.071)	0.151 (0.048)	<0.001

Annual Fitness was defined as an individual's contribution to population growth, and shown here are the phenotypic mean and the phenotypic (σ^2_P), year (σ^2_Y), permanent environment (σ^2_{PE}), maternal (σ^2_M), residual (σ^2_R), and additive (σ^2_A) genetic variances estimated under Model 1. Phenotypic variance (σ^2_P) was determined as the sum of estimated variance components. P values relate to the significance of σ^2_A on the basis of likelihood-ratio tests. Standard errors are provided in parentheses, nf indicates an effect not fitted, and $^+$ indicates a variance estimate fixed at the edge of parameter space (with nonestimable standard error).

correlations (r_G) between fitness at different ages remained close to +1 across much of the correlation surface, they reached values well below this when fitness in the youngest and eldest age classes was compared (Figure 3; minimum r_G: −0.16 in Soay sheep, ages 0 versus 10; 0.09 in red deer, ages 1 versus 15). Although there is little support for strong negative genetic correlations across ages, the fact that positive correlations decline might be indicative of some degree of antagonism between genetic effects on early and late fitness.

Eigenvector decomposition of the **G** matrices for age-specific p_{ti} also yielded similar results in the two populations (Table 2). The first eigenvector dominated in both cases (89.5% of the variance in sheep and 93.7% in deer) with loading coefficients of consistent sign that increased in magnitude across ages. This corresponds to variation in which an individual's additive genetic contribution to fitness is consistently either above or below the population mean at all ages. The increasing loading coefficients show that deviations from the mean increased with age (mirroring the trend of increasing σ^2_A). Although accounting for a comparatively small proportion of the variation (11.5% in sheep, 6.35% in deer), loading coefficients on the second eigenvector showed a switch in sign (Table 2), consistent with the occurrence of allelic variants that have a positive effect on early fitness and a negative effect later in life (or vice versa).

Two mutually nonexclusive genetic mechanisms have been proposed that could result from a weakening of selection late in life and be responsible for observed declines in fitness: antagonistic pleiotropy [3] (AP), and mutation accumulation [2] (MA). In the former case, senescence is the result of selection's favoring alleles with beneficial early life effects but detrimental consequences in late life. Under the latter mechanism, fitness declines result from a build up of deleterious mutations with effects specific to old age [1, 4]. Considerable efforts have been made to disentangle MA and AP as alternate genetic mechanisms in laboratory studies of senescence [8–10] and more recently in quantitative genetic studies of life history traits in natural populations [24–26]. However, it is important to note that although these are locus-based mechanisms, fitness, and quantitative traits closely correlated with it, is expected to be influenced by many genetic loci. If loci differ in their mechanism of contribution to senescence, then attempts to disentangle the relative roles of MA and AP will be methodologically challenging.

In the current instance, estimated **G** matrices for age-specific fitness show patterns of GxA that are consistent with a role for both genetic mechanisms. Thus, in both the Soay sheep and red deer, the dominant pattern was one of increasing additive genetic variance in later life, a pattern expected under MA but not precluded by the sole action of AP [2, 8]. Although few discriminatory tests are applicable outside of the laboratory, one expectation of mutation accumulation is that inbreeding depression will increase with age [8]. This derives from theoretical models as a consequence of increased sensitivity of fitness to homozygous recessive mutations in late life under MA but not AP [8]. We found some limited support for this relationship in the red deer population. Specifically, mixed-model analyses of p_{ti} (see Experimental Procedures) showed a negative, but nonsignificant, effect of increased inbreeding coefficient (F). However, the significant negative interaction between standardized age and F does indicate significant inbreeding depression at late ages (Table 3). It should be noted that power is limited here because only 4.5% of female red deer have $F > 0$. In the Soay sheep, the shorter life span coupled with a very low proportion of individuals having $F > 0$ (just 1%) meant this analysis of inbreeding effects had even less power. Nevertheless, negative coefficients associated with F and its interaction with age gave the same qualitative picture, albeit without statistical support (Table 3). Conversely, allelic variants with antagonistic effects on early and late fitness consistent with AP might also be segregating, as suggested by the declining genetic correlations and eigenvector analyses of the **G** matrices. Although this interpretation must be made cautiously, recent analyses of reproductive traits in the red deer provide additional support for antagonistic pleiotropy. For example, there is some evidence for a genetic basis to the observed trade off between early life fecundity and the rate of aging for offspring birth weight (an indicator of maternal performance [27, 28]). Genetic correlations consistent with AP have also been shown between shown early and late reproductive traits in mute swans (*Cygnus olor*) [26]. To the extent that patterns from these few study

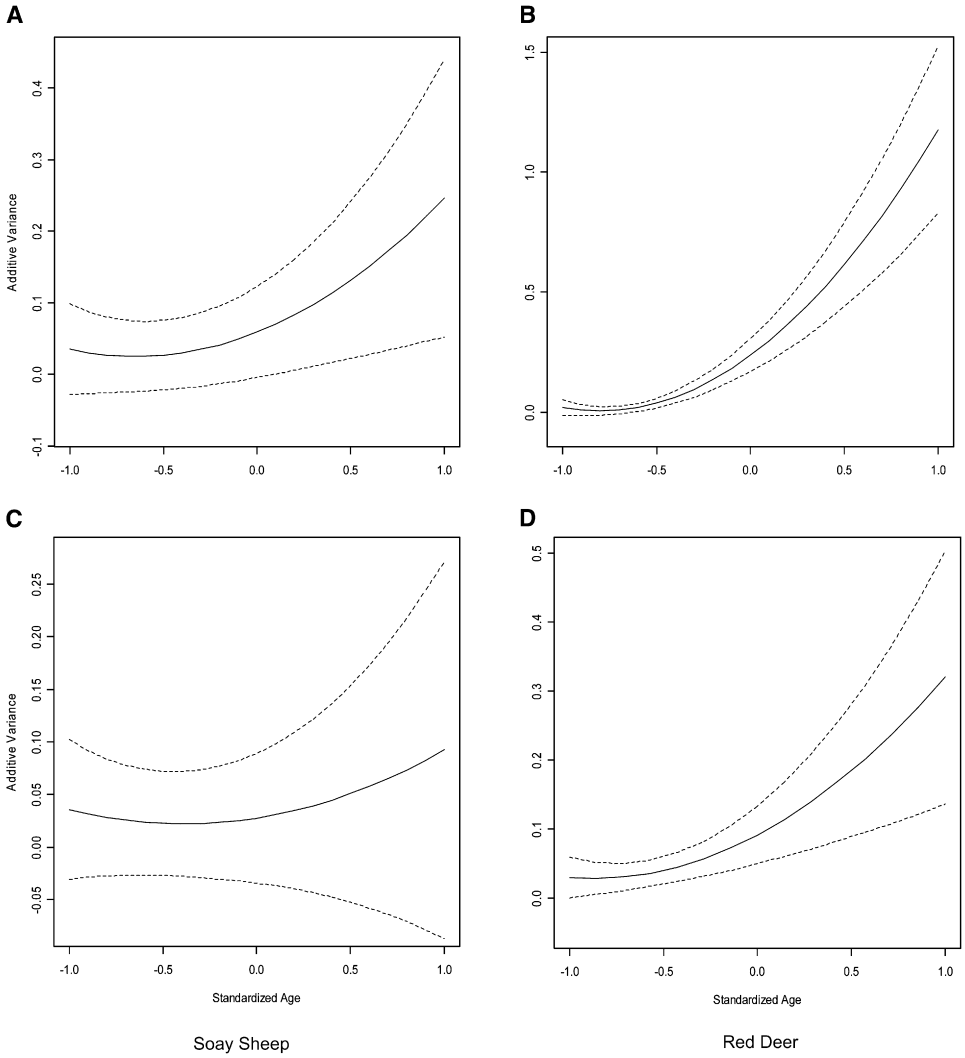

Figure 2. Additive Genetic Variance as a Function of Age in Soay Sheep and Red Deer

Additive genetic variance as a function of standardized age for annual fitness in sheep (A and C) and deer (B and D). The additive genetic functions were estimated under Models 2 (A and B) and 3 (C and D) (see text for details). Approximate 95% confidence intervals are shown by dotted lines. Note that the absolute (i.e., unstandardized) scaling of the age axis differs between plots (Soay sheep, 0–10 years; red deer, 1–15 years).

systems can be generalized, co-occurrence of MA and AP might therefore be the norm in natural populations, further confounding any attempt to separate them.

We have demonstrated here that aging processes measured at the phenotypic level also have an underlying additive genetic basis in wild animal populations. The presence of genotype-by-age interaction for fitness was statistically supported in the red deer, whereas analyses of Soay sheep were strongly suggestive of similar processes occurring. Recently, random regression animal models were also used for the exploration of the genetics of aging in a wild passerine bird [23]. In that case, the GxA term was not statistically significant, although when it was fitted, genetic variance for female fitness again increased with age [23]. There is a very real risk that power limitations inherent to data sets from natural populations will prevent detection of GxA, particularly for traits such as fitness that are expected to have low genetic variance. Appropriate tools for power analysis are now being developed [29] and should prove informative in this regard.

The genetic basis of senescence is a fundamental assumption of the evolutionary theory of aging that has, until now, remained largely untested outside of the laboratory [4]. The present study provides, to our knowledge, the first evidence for additive genetic variance in aging rates from a wild, nonmodel study organism. Furthermore, the age-specific patterns of additive genetic (co)variation evident in the two populations examined here were entirely consistent with the hypothesis that declines in fitness with age are driven by a weakening of natural selection. It should be noted that the assertion that natural selection must always weaken with age has been challenged by recent models [30]. If strong selection on the fitness of older animals were to arise in either the red deer or Soay sheep systems, then the increased additive genetic variance at late ages might facilitate further evolution of aging patterns (e.g, toward increased longevity [31]). It is therefore clear that a greater understanding of the evolutionary ecology of aging, and the implications of genotype by age interactions, should come from accurate

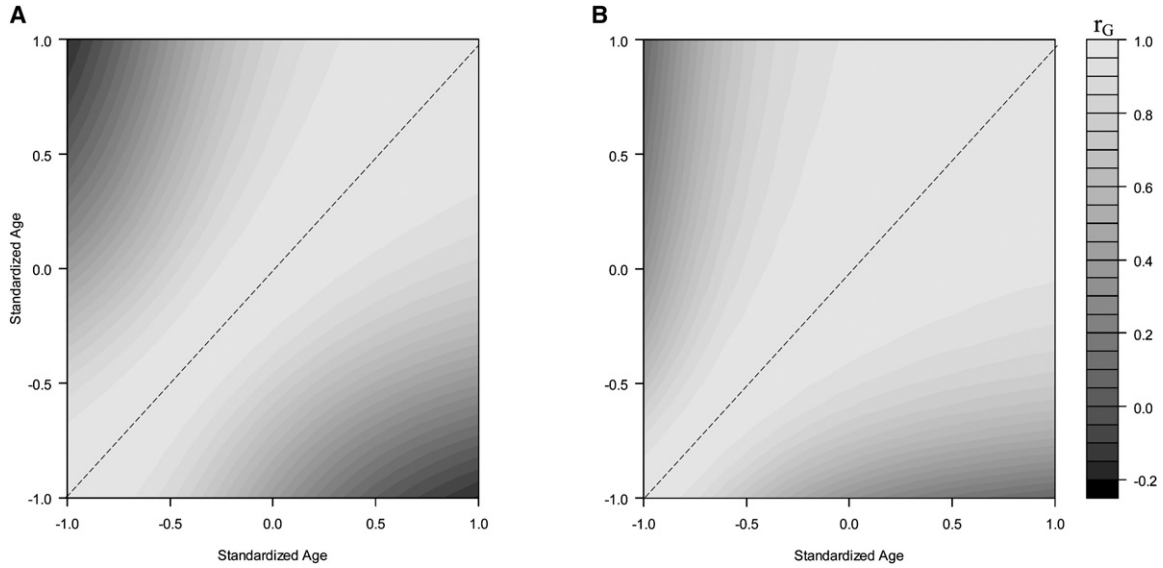

Figure 3. Genetic Correlations among Ages for Annual Fitness in Soay Sheep and Red Deer

Additive genetic correlation (r_G) structure across standardized age for annual fitness in (A) sheep and (B) deer estimated under Model 3. Standardized age is shown on x and y axes, with the value of r_G between any pair of ages denoted by the shading. Plots are symmetrical about the diagonal lines, where age on the x axis equals age on the y axis and r_G is thus defined as +1.

characterization of the **G** matrix for fitness (or fitness-related traits [32]) expressed across ontogeny. Our results give clear testimony to the importance and utility of long-term individual-based studies of wild populations for the testing of evolutionary theory in nature. It is our hope that similar analyses in wild populations will further elucidate the generality of the patterns observed here.

Experimental Procedures

Measure of Annual Fitness

We defined the annual fitness of individual *i* in year *t* as its contribution to population growth in that year (p_{ti}) [15]. This measure is appropriate for use in stochastic environments [15, 16], has distributional properties making it suitable for linear mixed-model analyses of the type performed here [17], and is defined as:

$$p_{ti} = \frac{s_{ti} - \overline{s_t}}{N_t - 1} + \frac{f_{ti} - \overline{f_t}}{N_t - 1}, \quad (1)$$

where N_t is the population size in year t, s_{ti} is the survival of individual i from year t to year $t+1$, f_{ti} is half of the number of offspring produced by i in year t that survive to year $t+1$, and $\overline{s_t}$ and $\overline{f_t}$ are the mean survival and fecundity for the population in year t, respectively. For computational purposes we rescaled fitness (multiplying by a factor of 1000) for all analyses, but for simplicity, we will nevertheless refer to this rescaled measure as p_{ti}. Population census data is collected at different times in the two studies, and consequently p_{ti} is defined for an annual period starting in August for sheep but in June for deer. This causes a slightly different partitioning of fitness, with first winter survival being allocated to the maternal f_{ti} in deer but to the offspring s_{ti} in Soay sheep. Analyses of Soay sheep data therefore include a 0 age class that is not present for red deer. Note that p_{ti} is also closely correlated with more traditional estimators of annual fitness, and qualitatively similar results (data not shown) were also obtained with annual fitness determined as survival (0 or 1) plus half of the number of recruits [23].

Soay Sheep

Since 1985, data relating to birth, death, and reproduction have been collected for individually marked Soay sheep (*Ovis aries*) resident in the Village Bay area of the island of Hirta (57°49' N, 08°34'W) in the St. Kilda archipelago of northwest Scotland. These data were used for the determination of p_{ti} for each female in each year of life. In total, 5663 estimates of p_{ti} were made on 1786 females. Sample sizes decline with age, from 1556 records at age 0 (i.e., fitness for the year commencing in August of the year of birth) to a single record at age 16. The pedigree structure of the population has been determined from field observations of maternity and microsatellite-based paternity analysis with CERVUS [33]. Putative paternal identities were accepted if assigned at $\geq$ 80% pedigree-wide confidence (subject to a maximum of one allelic incompatibility between sire and offspring). The full pedigree structure contained 6117 individuals, with 3355 maternal links and 1615 paternal links (from 784 distinct dams and 495 distinct sires, respectively), with a maximum depth of nine generations. Complete details of both field and laboratory procedures are presented elsewhere [12].

Table 2. Eigenvector Decompositions of the Genetic Variance-Covariance Matrices for Age-Specific Annual Fitness

	Soay Sheep (% Variation)		Red Deer (% Variation)	
Age	PC1 (89.5)	PC2 (10.5)	PC1 (93.7)	PC2 (6.3)
0	−0.012	−0.421		
1	0.027	−0.361	−0.031	−0.491
2	0.066	−0.300	−0.059	−0.438
3	0.105	−0.239	−0.087	−0.385
4	0.144	−0.179	−0.115	−0.333
5	0.183	−0.118	−0.143	−0.280
6	0.223	−0.058	−0.171	−0.227
7	0.262	0.003	−0.200	−0.174
8	0.301	0.064	−0.228	−0.122
9	0.340	0.124	−0.256	−0.069
10	0.379	0.185	−0.284	−0.016
11			−0.312	0.036
12			−0.340	0.089
13			−0.369	0.142
14			−0.397	0.195
15			−0.425	0.247

Loading coefficients on age-specific measures of annual fitness in Soay sheep and red deer are shown. In both cases, the **G** matrices were estimated under Model 3. Note that all variation is explained by two principle components because **G** is determined from the covariance matrix of random regression coefficients (having dimension 2).

Table 3. Mixed-Model Analyses to Test the Effect of Age on Inbreeding Depression

Population	Fixed effect	Coefficient (SE)	Numerator DF	Denominator DF	Conditional Wald F	P
Soay Sheep						
	Age		16	4657.0	69.06	<0.001
	F	−8.217 (6.283)	1	1806.0	0.97	0.329
	F. stAGE	−7.429 (6.940)	1	5008.0	1.15	0.283
Red Deer						
	Age		22	4780.8	33.23	<0.001
	F	−9.002 (4.414)	1	730.2	0.33	0.569
	F. stAGE	−11.010 (5.572)	1	4091.9	3.90	0.049

Models were fitted with fixed effects of age (as a factor), inbreeding coefficient (*F*), and the interaction between *F* and age (as a continuous variable). Individual identity was included as a random effect so that repeated measures on individuals could be accounted for, and the statistical significance of fixed effects was assessed with conditional Wald tests. DF indicates degrees of freedom.

Red Deer

Annual fitness was similarly determined for female red deer (*Cervus elaphus*) from the North Block of the Isle of Rum, Scotland (57°03' N, 06°21'W); this population has been studied intensively since 1971. The data comprised 5041 estimates of p_{ti} on 750 females, with sample sizes declining from 675 records at age 1 (fitness for the year commencing in May of the year after birth) to a single record at age 23. Maternities were determined by observation, whereas paternity assignment was based on a combination of molecular pedigree analysis and rut observations [34]. The full pedigree structure had 3740 individuals, with 3168 maternal links and 1262 paternal links (from 681 distinct dams and 243 distinct sires, respectively), with a maximum depth of ten generations. Full details of field and laboratory protocols used in this study are again presented elsewhere [17, 34].

Quantitative Genetic Analyses

We used animal models [20] to partition variance in p_{ti} into additive genetic and environmental components with the software ASReml 2.00a. Age-related patterns in additive genetic (co)variance were tested for in two ways. First, we estimated additive genetic variance in four age-specific data subsets of each population from Model 1,

$$p_{ti} = \mu + AGE + a_i + pe_i + m_k + year + e_i. \quad (2)$$

In sheep, data subsets were lambs (age 0), yearlings (age 1), prime age (2–4), and older (5+). In deer, they were were yearlings, second years, prime age (3–8), and older (9+). In Model 1, fixed effects included the population mean (μ) and age in years (as a multilevel factor). The distribution of individual breeding values (a_i) is assumed to have a mean of zero and variance of σ^2_A (the additive genetic variance). The estimation of σ^2_A is possible because the variance-covariance matrix of additive genetic effects is assumed equal to $\mathbf{A}\sigma^2_a$ (where **A** is the additive numerator relationship matrix obtained from the pedigree). Additional random effects were fitted for the avoidance of upward bias in σ^2_A from repeated measures and common environments [35] and included a permanent environment effect, pe_i (for prime age and older subsets); maternal identity, m_k; and year of measurement, *year*. Year was included so that the annual differences in important environmental conditions (e.g., density, weather, food availability) could be accounted for. All random effects (and residual errors, e_i) were assumed to be normally distributed (with zero means and variances to be estimated). For each data subset, statistical significance of σ^2_A was determined by likelihood-ratio test comparison to a reduced model. Significant differences in σ^2_A between prime-age and older animals were also tested for with bivariate formulations of Model 1 (but with no maternal effects fitted), in which p_{ti} in each age grouping was treated as a different trait. Likelihood-ratio tests were used for the statistical comparison of a model in which σ^2_A was free to differ between traits to a constrained model in which $\sigma^2_{A.\text{prime age}} = \sigma^2_{A.\text{older}}$.

The second approach we used was to explicitly test for genotype-by-age (GxA) interactions by using random regression [21, 36, 37]. Individual breeding values were modeled as linear functions of age, such that $a_{it} = a_{i0} + b_i.stAGE$, where a_{i0} is the additive genetic merit of individual *i* at *stAGE* = 0 and b_i is the slope of the individual's genetic reaction norm. To avoid extrapolating beyond the support of the data, we excluded records from females older than 10 years in the sheep and older than 15 years in the deer. This retained approximately 98% of available records in both cases. Thus, fitness of individual *i* at time *t* (Model 2) was specified as

$$p_{ti} = \mu + AGE + (a_{i0} + b_i.stAGE) + pe_i + m_k + year + e_i. \quad (3)$$

Because there was a lack of support for maternal effects in deer or sheep older than 0 (Model 1 results), we specified the maternal effect m_k to be present only in Soay lambs. Significance of GxA was assessed by likelihood-ratio tests to a reduced model in which the additive effect is a zero-order function of age (i.e., constant). Variance-covariance matrices for a_{i0} and b_i were back transformed to give **G**, the additive genetic covariance matrices of age-specific fitness and approximate standard errors estimated (in accordance with [38]). We used eigenvector decomposition to summarize the major patterns of variation in **G**.

Although σ^2_A can change with age under Model 2, other variance components are constrained to be constant. Assuming such homogeneity might not always be appropriate [39], we therefore also tested models, with pe_i also treated as a first-order function of age. This did not significantly improve the model for either population (data not shown). Second, we relaxed the assumption of homogenous residual variance by fitting error structures as diagonal matrices with dimension equal to the number of age classes (Model 3). Although requiring a large increase in the number of parameters to be estimated (an additional 11 in sheep and 15 in deer), this structure allows residual variance to vary with age.

Age-Specific Effects of Inbreeding Depression

We tested for increased inbreeding depression with age [8] by using mixed models of p_{ti}. The inbreeding coefficient (*F*) of each individual was obtained with the program Pedigree Viewer (http://www-personal.une.edu.au/~bkinghor/pedigree.htm), and both *F* and its interaction with *stAGE* were fitted as fixed effects. A main effect of age (as a factor) was also included, and identity and year of measurement were included as random effects. Parameter estimates were obtained with the program ASReml 2.00a, and the significance of fixed effects determined from conditional Wald F statistics.

Supplemental Data

Two tables are available at http://www.current-biology.com/cgi/content/full/17/24/2136/DC1/.

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